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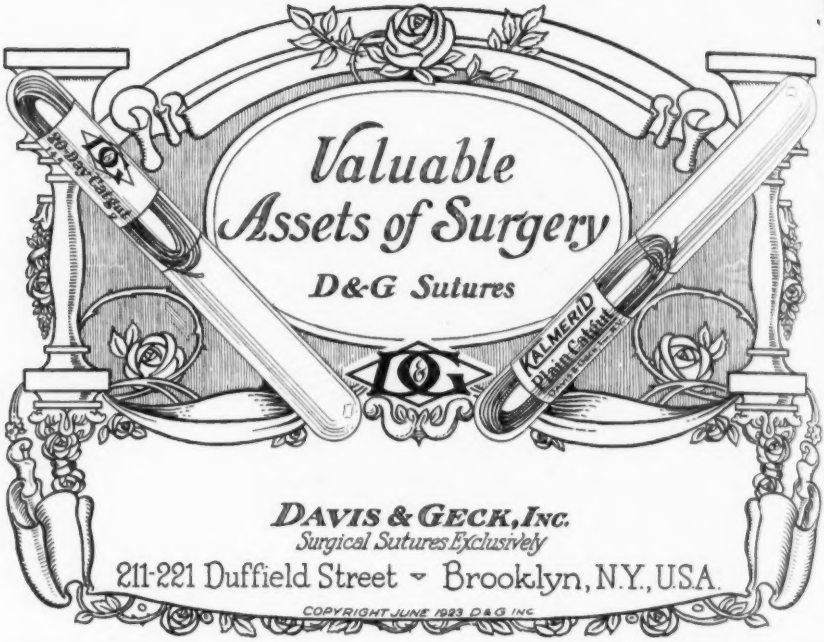

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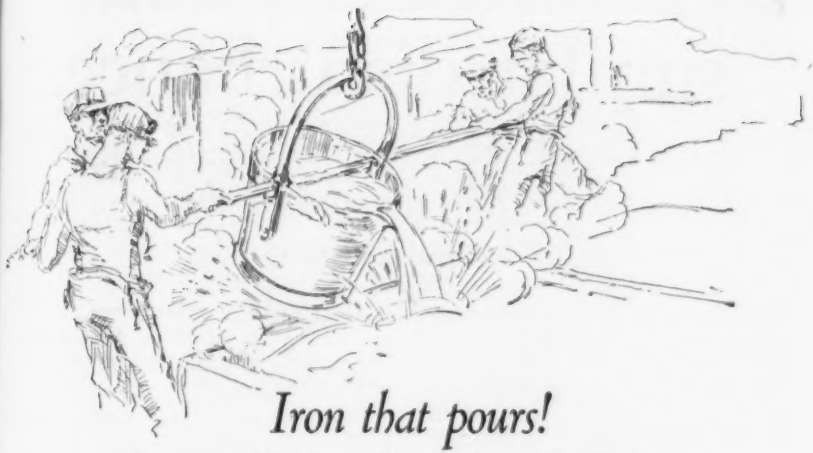

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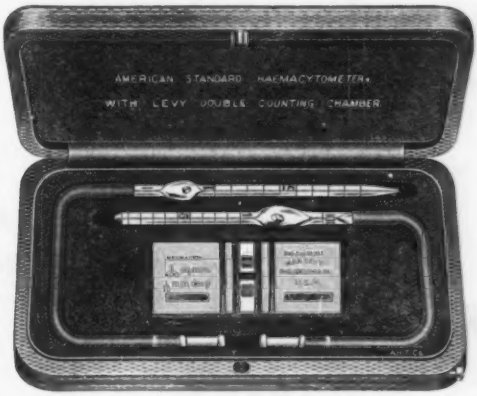

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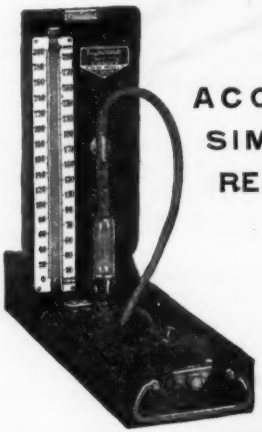

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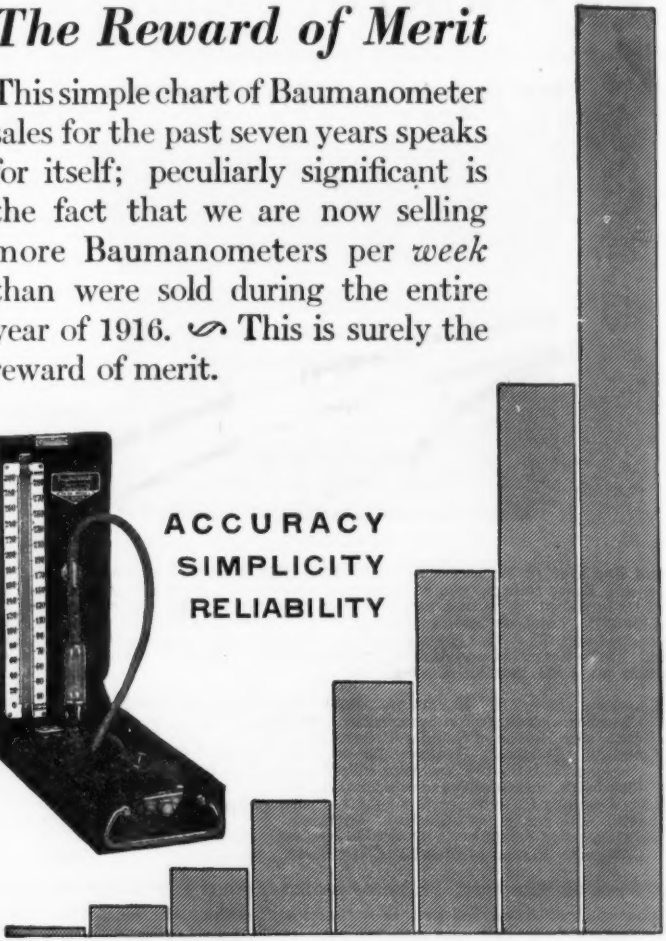

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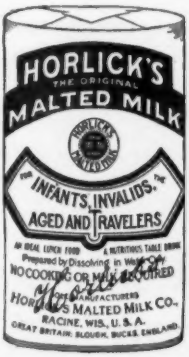

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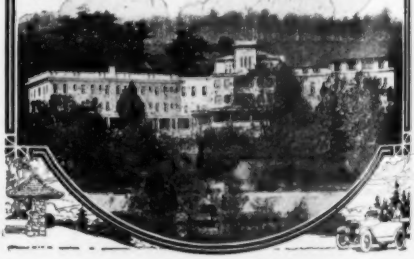

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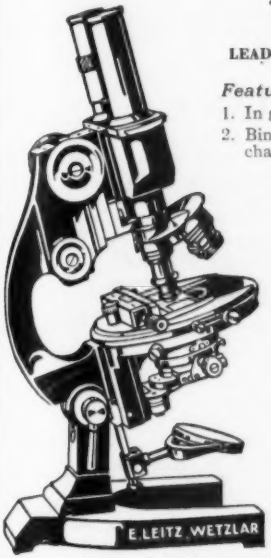

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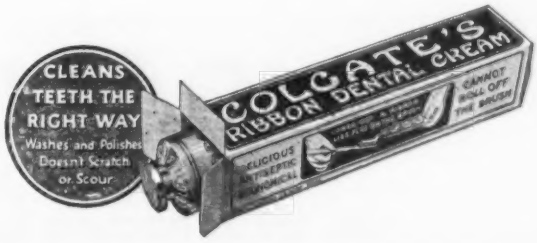

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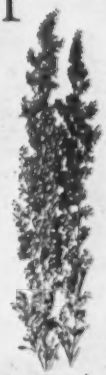

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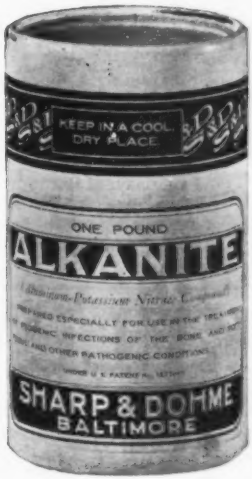

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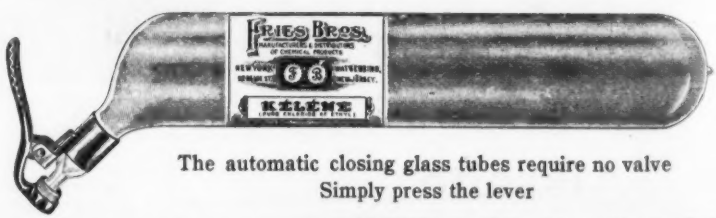

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JUNE, 1923

ORIGINAL ARTICLES.

ON SUBCUTANEOUS FIBROID NODULES IN RHEUMATISM.

By E. Bronson, M.D.,

and

E. M. Carr, M.D.,

With a Pathological Report of One Case,

By W. A. Perkins, M.D.,

San Francisco, Calif.

(From the Pediatrics Department of the University of California Hospital and from the Children's Hospital, San Francisco.)

The subcutaneous nodule, as a sign pathognomonic of rheumatic fever, has until recent years scarcely been considered by the American pediatrician. Brennemann,[1] in 1919, published observations on the incidence of these nodules in Chicago. He has given such a clear word picture of them, their size and location, that we need not repeat. He has also summarized their treatment, or rather lack of treatment, by American text-books of pediatrics. The purpose of our paper is to call attention to the fact that fibroid nodules are a frequent accompaniment of severe rheumatic infection in San Francisco, as well as in Chicago and Great Britain, and to emphasize that they are not to be classed as a medical curiosity, but that they are one of our most valuable diagnostic and prognostic signs in rheumatic fever.

Mitchell,[2] in 1888, from Osler's Clinic in Philadelphia, was the

[1] Am. Jour. Dis. Child., 1919, **18**, 179.
[2] Univ. Med. Mag., 1888-9, **1**, 161.

first to report a case in this country. Futcher[3] also, under the inspiration of Osler, quotes the latter as of the opinion that rheumatism occurs much less frequently in Philadelphia and Baltimore than in London, and that the subcutaneous fibroid nodules as a complication of rheumatism are "a great rarity" in the former two cities. It must be recalled, however, that Osler worked chiefly with adults while the British observations were mainly in children and adolescents. In Futcher's paper, Davaine is given as authority for the statement that nodules were known as early as the latter half of the 18th century. Futcher also states that they were associated first with rheumatism in 1843 by Froriep. Hillier,[4] in 1868, appears to have been the first to publish an instance of their occurrence in England. His observations were independent of those previously made on the Continent. In 1871, Jaccoud[5] described fully their character and location. He had seen them in four cases but regarded them as rare.

The paper by Barlow and Warner,[6] at the Seventh Session of the International Medical Congress, 1881, remains to the present the classical exposition of this subject. Their observations over a period of six years were undoubtedly known to their associates before publication. Their paper was followed by Cheadle's delightful lectures on rheumatism, and thereafter references to rheumatic nodules in British literature became frequent, and the search for nodules, a matter of routine in the examination of the rheumatic child.

Casual references to fibroid nodules are seen occasionally in our journals, sometimes with an unfortunate ambiguity. Riesman,[7] in an otherwise excellent summary of rheumatism, characterizes them in one instance as follows: "Closely aggregated over the buttocks were innumerable reddish papules, pea size and larger, with very little intervening normal tissue. They were movable, not tender and gave the buttock a pebbly feel and appearance. Nodules of smaller size were present on the legs. In addition, there were scars of the same size as the papules scattered over the arms and thighs." This description suggests one of the erythemas not infrequently associated with acute rheumatism, not the fibroid nodule of Barlow and Warner.

On the finding of nodules in several instances, soon after the arrival of one of us* in San Francisco, the suggestion was made that we were dealing with a more severe type of rheumatic infection than was usual in this part of the country. To evaluate this

[3] Bull. Johns Hopkins Hosp., 1895, **6**, 133.
[4] Diseases of Children, Philadelphia, 1868, p. 249.
[5] Traité de Pathologie interne, Paris, 1871, **2**, 546.
[6] Tr. Seventh Internat. Med. Cong., London, 1881, **4**, 116.
[7] Jour. Am. Med. Assn., 1921, **76**, 1377.
* E. B. has to thank Dr. John Thomson of Edinburgh and Dr. G. A. Sutherland of London for calling her attention to this manifestation of rheumatism.

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criticism and to estimate how much emphasis is ordinarily put upon this rheumatic sign, we have reviewed the histories of the Pediatric Department of the University of California Hospital from 1914 and of the Children's Hospital from 1917 and analyzed the rheumatic cycle cases. We have separated the cases into those seen before our own observations began and those followed by us. Brief notes on the latter series are tabulated below. We have classified both series, according to our estimation of the severity of the damage following the rheumatic infection, into three groups: Group I, children leaving the hospital with apparently complete recovery or with a slight systolic blow only and no obvious functional disability; Group II, those with a definite carditis but from whom, presupposing no fresh rheumatic infection, one can prognosticate a fairly normal active life; Group III, those with a crippling carditis, such as a progressive mitral stenosis, signs of adherent pericardium, extreme ventricular hypertrophy, as well as those already having the symptoms of chronic cardiac failure.

We realize that in such an arbitrary grouping the personal equation has played an important part. The best of histories does not always give an accurate estimate of the severity of an infection. If we had accepted the diagnosis of mitral stenosis or the mention of a "presystolic murmur and a roughened first sound" as the equivalent of a stenosis, each time so noted, Groups II and III, would have been much greater. We have omitted entirely a considerable number of cases of tonsillitis diagnosed as "mitral disease" on the presence of a slight systolic blow at the apex. In formulating the table we decided that a brief summary of the physical signs would be the simplest and most advantageous method of stating the facts of the history. It will be noticed that cardiac function is relegated to the background and physical signs unduly emphasized. Any other attitude would have been difficult, utilizing routine hospital records. If the history did not mention chorea, we have assumed this to be absent. The omission from our table of a routine reference to tonsillar infections may be criticized. In our experience there has been no correlation between tonsillar involvement and the sign of rheumatic fever which we are discussing. In our "Remarks" column we have endeavored to call attention to instances of infection of a severity which we believe predisposes to the presence of nodules. We have added the group classification, made on as nearly as possible the same basis as we used in the series of cases not seen by us.

These tables are a record of 38 children whom we had the opportunity of observing. We have grouped them as follows:

Group I, 12 cases, or 31.6 per cent, only 1 of whom showed nodules.

Group II, 9 cases, or 23.6 per cent, 3 of whom had nodules.

Group III, 17 cases, or 44.7 per cent, 13 of whom had nodules.

Seven of Group III died and 6 of the 7 showed nodules. Of the total 38 we found nodules on 17, or 44.7 per cent.

TABLE OF RHEUMATIC CYCLE CASES SEEN BY BRONSON AND CARR BETWEEN SEPTEMBER, 1919, AND SEPTEMBER, 1921.

Year, No.	Case record, No.	Age, sex.	Arthritis.	Carditis.	Chorea.	Nodules.	Remarks.
1919 1	R. L. 5190	12 M.	No history.	Systolic murmur which disappeared while under observation.	Severe attack tending to become chronic.	None.	Complete recovery under reëducative treatment. Group I.
2	R. P. 2329CH*	12 F.	First attack 1 week before entrance; extensive involvement including small joints.	Heart much dilated, loud systolic blow; developed stenosis and pericarditis; general cardiac failure.	None.	In third week of illness large nodules noted on elbows, patellæ, occiput and spinous processes.	A severe infection with recurring arthritis, tonsillitis and crops of nodules; progressive carditis; death in 2 months; no necropsy. Group III.
3	M. L. 2325CH	12 F.	First attack 4 years, second attack 1 year before entrance. Entered during third acute attack.	Aortic diastolic murmur; mitral systolic blow; cardiac hypertrophy; friction rub of a few days' duration.	None.	During acute attack small nodules on elbows.	In hospital 6 months with slow but steady improvement; has been under constant observation up to present; goes to school and leads fairly normal life; has developed little or no stenosis; shows left ventricular hypertrophy. Group III.
4	G. J. 2309CH	12 M.	Definite attacks 8 years and 5 years before entrance; several other mild attacks; none on admission.	Heart enlarged; loud systolic murmur.	None.	None.	Present admission for acute nephritis; apparently not related to rheumatic infection. Group I.
5	E. C. 2310XCH	10 M.	Five previous mild attacks. Entered during sixth.	Systolic and presystolic murmurs; no fresh cardiac involvement.	None.	None.	Two previous admissions to University Hospital No. 10679 and No. 11642; second admission 1916 for chorea, at which time nodules stated absent. Little change in cardiac condition since first admission in 1915. Group II.
6	E. M. 5437	12 M.	Definite attack 2 months before entrance. Convalescing on admission.	None.	None.	None.	Made rapid, complete recovery. Group I.
1920 7	L. B. 5935	10 M.	Entered during acute attack; no previous attack.	Systolic murmur; no other abnormal cardiac findings.	None.	None.	Recovered in 1 month with little if any permanent damage. Group I.
8	G. F. 6573	14 M.	First attack 5 years before admission. Entered during second with moderate joint involvement.	Heart enlarged; systolic and diastolic murmurs at apex and base; later developed presystolic murmur.	None.	None noted on entry; 3 weeks later on head, spinous processes, scapulæ and elbows.	Previous entry No. 11005; nodules at that time persisting throughout 2 months' stay in hospital. On present admission an extensive, typical erythema rheumatica circinata. This disappeared and recurred during observation; reëxacerbation of pharyngitis, arthritis and carditis during 3 months' course; discharged little improved. Group III.
9	F. F. 6864	5 F.	Mild attack one month before entrance. No involvement on admission.	Blowing systolic murmur over precordium.	None.	None.	Severe tonsillar infection with definite arthritis and very little cardiac involvement. Group I.

* CH refers to cases from the Children's Hospital. The cases not thus denoted are from the Pediatrics Department, University Hospital.

10	L. K. 9887	10 F.	First attack began 3 months before entrance. Entered during exacerbation.	Systolic murmur and enlarged heart on admission; later developed precordial friction and apical diastolic murmur.	None.	Three weeks after entry appeared on occiput, scapulæ, elbows and knuckles. Photograph No. 1.	Temperature 40° C. on admission; several exacerbations of temperature and arthritis during course of 6 weeks in hospital. A steadily progressive carditis; successive crops of nodules; removed against advice and died following month. Group III.
11	F. R. 7269	9 M.	First attack 2½ years before admission. Entered during second attack.	Blowing systolic murmur. No enlargement.	None.	None.	Recurring joint pains with slight elevations of temperature; discharged after 6 weeks much improved but with persisting systolic blow. Group I.
12	H. M. 7441	8 M.	Entered during first attack 1 month after onset.	Soft systolic murmur on admission; developed pericardial friction and effusion. Pancarditis.	None.	Developed on head and elbows 5 weeks after onset of arthritis; later on spinous processes and patellæ. Photograph No. 2	Progressive rheumatic infection terminating in death from cardiac failure; no necropsy. Group III.
13	D. S. 8416	10 F.	Three severe attacks in past 6 years; frequent indefinite joint pains; no acute attack on entrance.	Hypertrophied heart, systolic refraction at apex, presystolic rumble, loud systolic blow.	With first attack of arthritis.	None.	Three previous entries No. 10094, 13215 and 16273. Nodules not mentioned; followed by us since latest admission; marked impairment of cardiac function but no arthritis and no nodules. Group III.
14	F. B. 9677a	11 F.	First attack 4 years before admission. Entered during second acute attack.	Heart greatly enlarged; systolic murmur at apex, systolic and diastolic at base; later pericardial and pleural effusions.	With first attack; duration 3 months.	On dorsum of feet and elbows.	High septic temperature, progressive carditis, death from cardiac failure after 2 months in hospital; no necropsy. Group III.
15	L. B. 2327CH	11 M.	First attack very severe, 3 years before entrance and second 1 year before entrance. Entered during third attack.	Heart greatly enlarged; loud systolic blow at apex; later developed typical aortic diastolic at base.	None.	None.	Cardiac function excellent when seen 5 months after leaving hospital. Group II.
16	V. A. 2304CH	11 F.	First attack following tonsillectomy 3 years before admission. Entered after second attack.	Soft systolic murmur which disappeared before discharge.	None.	None.	A mild rheumatic attack with apparently complete recovery. Group I.
17	F. W. 2321CH	10 F.	First attack 2 years before entrance; in bed 6 months. Entered during second attack.	Heart enlarged; booming first sound and loud systolic blow; later developed apical diastolic.	None.	None.	In hospital 2½ months; since discharge has had several attacks of arthritis and is reported to have mitral stenosis; no nodules at any time when seen by us. Group II.
18	W. W. 2311CH	11 F.	Entered during first attack, 3 weeks after onset.	Soft systolic apical murmur on admission, later developed into a well-transmitted murmur of valvulitis.	None.	None	Onset with severe tonsillar infection; rapid recovery from arthritis with very little carditis on discharge. Group I.
19	A. G. 2322CH	13 M.	First attack 5 months before entry. Subacute arthritis throughout course in hospital.	Systolic and diastolic murmurs on entrance; developed pericardial effusion and extreme cardiac hypertrophy, with definite aortic valvulitis.	None.	None.	Under observation in hospital for 6 months with signs of cardiac incompetence; died suddenly at home soon after leaving hospital; no necropsy. Group III.
20	A. N. 2324CH	11 M.	None.	Slight transient systolic blow.	Severe attack of 4 months' duration.	None.	Made complete recovery. Group I.
21	E. G. 2315	13 F.	None.	Systolic blow one week after onset of chorea.	Extremely severe attack.	Two weeks after onset of chorea nodules developed on spinous processes, scapulæ, elbows, left hamstring tendon.	On admission had a typical erythema rheumatica circinata on extensor surfaces of arms. This later appeared on chest and upper abdomen; when seen July, 1921, definite signs of beginning stenosis were present; she reports that she has not been free from nodules since discharge from hospital one year ago; small sago-like nodules on elbows and tendons of wrists. Group III.

TABLE OF RHEUMATIC CYCLE CASES SEEN BY BRONSON AND CARR BETWEEN SEPTEMBER, 1919, AND SEPTEMBER, 1921.—(*Continued.*)

Year. No.	Case record, No.	Age, sex.	Arthritis.	Carditis.	Chorea.	Nodules.	Remarks
22	J. M. 2336CH	13 M.	First attack 3 years, second attack 6 months before admission; none on entrance.	Musical systolic murmur noted after first attack; pericarditis with second; cardiac failure with general anasarca on entrance.	None.	None.	Left hospital after 2 months with mitral stenosis, adherent pericardium and extreme ventricular hypertrophy; under observation up to present; no nodules at any time. Group III.
23	A. L. 4039CH	10 M.	First attack 4 years before admission. Entered during second attack.	Heart enlarged; blowing systolic murmur.	None.	On admission large nodules on elbows.	Previous admission No. 11428; nodules not mentioned; 6 weeks in hospital on present entry; no arthritis since discharge; seen June, 1921, when he had definite presystolic rumble and other signs of developing stenosis; large nodule on right olecranon and small ones on left olecranon. Group II.
24	W. I. 6168	12 F.	None on first entry; subacute joint pains for past year; acute attack 2 weeks before admission.	Slight systolic blow on first admission; on second pancarditis developing pericardial adhesions and stenosis. Definite signs of aortic insufficiency.	In hospital with acute attack one year ago; duration one month; none on present entry.	Present on re-admission; recurring crops on elbows, wrists and spinous processes.	Previous entry No. 6168 for mild chorea; during second stay in hospital, through a period of 7 months, recurring pharyngitis and subacute arthritis with elevations of temperature; fresh crops of nodules with each exacerbation, though improved ultimate prognosis bad. Group III.
1921 25	C. I. 10582	14 M.	First attack 1½ years before entry. Entered during second attack.	Apical systolic murmur; diastolic murmur at base; question of adhesive pericarditis.	None.	None.	Left hospital after 4 months with definite carditis but with good cardiac function. Group II.
26	C. L.	12 F.	Entered during first attack.	Dilated heart, loud systolic blow; later developed basal diastolic.	None.	None.	Still under observation in hospital; onset of arthritis accompanied by unusually severe tonsillitis. It is impossible at present to say how much cardiac damage will result. Group II.
27	S. M.	10 F.	Several subacute attacks. Entered during latest.	Soft systolic blow at apex.	None.	Small nodules on elbows, occiput and spinous processes.	After one month's observation with no joint symptoms no elevation of temperature over 1° and a mild carditis, patient continued to develop nodules. Were it not for the presence of nodules an excellent prognosis could be given. Group I.
28	D. O'C. CH	7 F.	First attack one year, second 8 months before admission. Entered during third attack.	Loud blowing, systolic murmur and dilated heart on admission; developed presystolic murmur and booming first sound; acute pericarditis second month in hospital.	None.	On both elbows on admission; later developed on spinous processes, tendons of hands and feet and on scapulæ.	Recurring subacute attacks of arthritis throughout 3 months' stay in hospital; severe carditis, steadily progressing stenosis and probably adhesive pericarditis; crops of large nodules. Group III.
29	A. J. CH	4 F.	Entered during first attack.	Soft systolic blow which progressed into a loud musical murmur; booming first sound; no definite presystolic rumble.	None.	A few small nodules on elbows appeared 2 weeks after onset. These have persisted during past 4 months.	No recurrence of arthritis, yet a gradually increasing cardiac involvement. Group II.

30	S. S. CH	6 F.	Entered during first attack; very severe.	Very rapid heart; weak first sound; soft systolic blow on admission.	None.	None.	Apparently made a complete recovery within one month from onset. Group III.
31	I. D. CH	9 F.	Entered 2 weeks after onset of first attack; joints much swollen, red and fluctuant; very extensive involvement.	While under observation developed systolic blow with slight enlargement and weak first sound.	None.	Three weeks after onset of arthritis nodules appeared on elbows. These increased in size and others appeared on occiput and hands.	A very striking erythema rheumatica circinata and severe tonsillitis a few days after admission. After 10 months of observation is still having exacerbations of arthritis and crops of nodules; progressive carditis. Group III.
32	S. M. CH	12 M.	Entered during first attack one month after onset.	Systolic murmur which has persisted until present time.	None.	None.	Severe arthritis but with rapid improvement; under constant observation. Group I.
*33	M. P. CH	7 F.	First attack 5 years, second 1 year before admission; both severe; recurring joint pains.	Hypertrophied and dilated heart; signs of mitral stenosis and adherent pericardium.	None.	Large nodules on both elbows, spinous processes, scapulæ and wrists.	Symptoms of moderate cardiac failure while in the hospital; a very crippled heart becoming progressively worse. Group III.
†34	J. B.	12 M.	First attack in Italy 6 years ago; in bed 9 months; recurring attacks since, number not known; frequent joint pains.	Extreme cardiac enlargement; presystolic rumble and systolic blow at apex, in aortic area systolic thrill and very rough murmur; diastolic of typical aortic quality.	None.	Large nodules on elbows, forearms, knuckles, spine, knees, and head.	A circinate erythema seen by one of us before admission. Patient states he has had nodules for at least 1 year; suffering from chronic cardiac failure. Death in hospital, necropsy. Group III.
35	P. S.	9 M.	Recurrent attacks for 4 years; none on entrance.	History of murmur with first attack of arthritis; heart enlarged, systolic and presystolic mitral murmurs.	Severe attack started 2 months before admission and still present.	None.	A moderately severe chorea tending to become chronic; definite carditis. The type of case in which one would expect nodules to develop. Group II.
36	W. G.	7 M.	Joint pains for 2 months; no severe attack.	Heart enlarged; signs of beginning stenosis but too early in course to predict amount of permanent cardiac damage.	Severe attack started 2 months before entry and still present in hospital.	On occiput one very large nodule with many small ones, large ones on elbows, wrists, scapulæ, tibiæ, patellæ, ankles and spinous processes.	The nodule on the occiput appears to measure 2 cm., but on examination the size is probably due to indurated subcutaneous tissue over a conglomeration of small nodules. The tumor as a whole is soft, the nodules themselves are hard. Group II.
37	J. P. CH	10 M.	None.	Systolic murmur at apex.	First attack 1 year and second 1 week before admission.	None.	Apparently making a complete recovery; still under observation. Group I.
38	H. M. CH	5 M.	Onset of first attack 8 weeks before admission; none on admission.	Extensive pericardial friction rub; pancarditis; extreme dilation and cardiac failure.	None.	Noted by mother soon after onset; large nodules on occiput, spinous processes, elbows and knuckles.	A very severe acute carditis; died second day in hospital; no necropsy. Group III.

* Death occurred after completion of table, hence this case is not counted in our mortality statistics.
† For pathological report on No. 34, see text.

In the pediatric records of the period before our observations began we have found 45 admissions of rheumatic cycle cases. Four of these were readmissions which we have counted because they were fresh opportunities for the search for nodules. Moreover, in such recurring attacks one is the more likely to encounter nodules. An example is A. L., No. 23 in our table, who has not been without nodules during the nine months we have observed him, yet in whose history for a former admission nodules were not mentioned. D. S., No. 13 in our table, examined at frequent intervals for a year, has had no exacerbation of rheumatic infection and no nodules, though severe cardiac injury. During her preceding hospital admissions she was suffering from some acute phase of rheumatic fever, and at least in a condition to predispose to nodules.

In these 45 histories of rheumatic cycle cases admitted before our series began, nodules were not mentioned in 41, stated absent in 2 and stated present in 2. We have classified the 41 individuals who comprised the 45 admissions as Group I, 23, or 56.1 per cent; Group II, 9, or 21.9 per cent; Group III, 9, or 21.9 per cent. Of the 2 cases in whom nodules were found, 1 was G. F., No. 8 of our own series. Though according to the record of his former admission he is placed in Group II, the present degree of cardiac damage changes him in our series to Group III. Of the other case, T. B., 5122 C. H., the history states, "The mother noticed during the present illness that the child had some small, hard lumps developing upon head and elbows." A careful record was made of these in the hospital. Death occurred two months after these notes were made.

At a glance it would appear that there had been an epidemic of rheumatic fever during the past two years. Of our 38 cases, however, only 14, or 38.8 per cent, were first attacks. Several factors contribute to our comparatively large series. The Pediatric Service of the University Hospital has grown rapidly during recent years. A yearly variation in rheumatic cycle cases is shown, but certain preceding years have a higher ratio to total admissions than has been present during the period we have covered. It should be noted also that the Children's Hospital series begins only in 1917. Another reason for our numbers has been the kind coöperation of our colleagues in affording us an opportunity to examine the largest possible number of cases. We have been invited to see a greater number of severe than mild cases, a factor which has probably swelled the proportion in Group III.

Though our own series shows a greater percentage of severe infection, there are instances in the former histories which parallel certain of ours in the amount of carditis and termination by death. G. A., University of California Hospital, No. 8032, who ran a progressive and finally fatal course in eight months from the onset of

the first symptoms, is an example. Fibroid nodules were not mentioned in his history. That nodules are not a necessary accompaniment of fatal cases is shown by the record of A. G., No. 19 of our series, who on no occasion showed them during six months in hospital. He died a month after he was discharged. During the period under observation, however, he was suffering from symptoms of cardiac failure, and at no time had any acute arthritis or fresh cardiac infection. Several of Group III we have followed for nearly two years, at no time finding nodules. They are suffering from inefficient hearts, not from any exacerbation of rheumatism. Such instances illustrate the general fact that the nodules are a sign of some active rheumatic focus, and that they tend to disappear as the infection becomes quiescent. We do not wish to be misinterpreted on this point. Nodules infrequently accompany the high initial fever and stage of swollen joints, circinate erythema, and other signs of acute rheumatism. A reference to our table will show that in our experience they are demonstrable ten days to two weeks from the onset, that is, at the time the more obvious arthritic signs are subsiding, and when a carditis is to be expected. Our observations are in sufficient contrast to the history records of preceding years to justify the statement that in San Francisco the search for nodules has not been a part of the routine in investigating the rheumatic child, or that during the past two years an unusually severe type of rheumatic fever has occurred in this locality.

To reiterate, rheumatic nodules are fibroid tumors varying from the size of a grain of sago to one or more centimeters in diameter. These apparently large nodules are often conglomerations of smaller units. Frequently in a place irritated easily, as the olecranon process or the occiput, the nodules appear much larger than their actual size, due to a chronic thickening of the subcutaneous tissues over and about them. This thickened tissue may be fairly freely movable and should not be confused with the underlying nodules. The nodules themselves are attached to tendon sheaths and aponeuroses. Their movability varies with the tissue to which they are attached. The skin moves freely over them. They are not tender, unless by exigency of size and location, stretching of surrounding tissue occurs. They are not reddened unless by external injury. Their disappearance is macroscopically complete, leaving no discoloration. Early in their development a useful method of detecting them is by moving the skin back and forth over the suspected area. They will appear as little elevations often a bit shiny, not moving with the skin. To verify the presence of a nodule over a bony point, one may compress it between the nails of the forefingers. Even a small nodule gives a feel different from skin and subcutaneous tissue. The growth of individual nodules and the appearance of fresh crops may be

rapid, and their disappearance equally so, or they may persist month after month without striking changes.

Histologically, according to Coombs,[8] they are composed of a groundwork of fibrin with multinuclear fusiform cells, together

FIG. 1.—L. K., No. 10 of our series.

FIG. 2.—H. M., No. 12 of our series.

with leukocytes and plasma cells. Barlow and Warner regarded them as "organizing granulation tissue, homologous with the

[8] Jour. Path. and Bacteriol., 1910, **15**, 489.

inflammatory exudate forming the basis of vegetation on the cardiac valves." According to Coombs and also Jacki,[9] their structure more closely resembles that of the Aschoff bodies in the heart muscle, and, like the latter, they represent a local tissue reaction to the unknown etiological agent of rheumatic fever.

We were able to secure only one necropsy, J. B., No. 34 of our series.

History. An Italian boy, aged eleven years, who came to America one year before his final illness.

Family History. Father and mother and three other children are fairly healthy. No other rheumatic incidence.

Past History. Since he was left in Italy when his people came to this country, the history was obtained chiefly from the boy himself. He stated that his first attack of rheumatism (swollen joints) was seven years ago, when he was kept in bed nine months, and was very ill. He had seven other attacks of arthritis before coming to this country. Once for a few weeks he had, apparently, chorea. He denied ever suffering from sore throat. His relatives stated that the nodules on his elbows had been present on arrival to this country.

Present Illness. He was first seen by one of us (E. B.) July 2, 1921, walking into the office, though looking a very ill boy. He had no fever. He had been in a San Francisco hospital for one month and discharged improved about two weeks previously. The instructions given him had been entirely disregarded, with a rapid return of the signs of cardiac failure. He complained especially of sharp pains occurring almost daily over his left upper chest and inability to sleep.

The signs of venous engorgement in the neck were extreme. His body moved with each cardiac contraction. The carotid and brachial pulsations were visible at a distance, and the blanching and reddening of the lips and nails needed no tests for elicitation. Visible cardiac fluttering impulse and retraction from the third interspace at the right of the sternum to the sixth interspace on the left measured 25½ cm. The ankles pitted on pressure. There was no tenderness. The liver reached nearly to the umbilicus. The pulse counted 148 and was typically aortic. Respirations, 64. Over the aortic area was felt a very striking thrill. None was found over the apex beat. At the apex the first sound was weak rather than exaggerated, and had a gallop rhythm. The second sound was also poorly differentiated. There was a systolic-diastolic blow of no great intensity, and no presystolic rumble. In the aortic area the first sound was accompanied by a rumbling, rough systolic murmur. The second sound was exceedingly sharp and

[9] Frankfürter Ztschr. f. Path., 1919, **22**, 82.

ended in a diastolic blow of typically aortic quality. No extracardial murmur was heard. Though retractions of the interspaces over the precordium accompanied the apex impulse, no retraction of the interspaces over the back could be made out.

Rheumatic nodules of moderate size were present over elbows, knuckles of fingers and spinous processes. There were none over knees and head. He thought they had been bigger than at present.

Progress. Hospital care was refused. He was put to bed and kept quiet with codein. Free catharsis was used. In two days the heart rate dropped to 110 and respirations to 30 to the minute. The venous enlargement in the neck had decreased, and the liver was nearly up to the costal margin. The third day a circinate erythema of rheumatic type appeared, and he complained of pain in knees and ankles, and tenderness to touch. His temperature was around 38° C. No fresh nodules were found.

His family were finally persuaded of the necessity of hospital care, and he was referred to the Children's Hospital, on the service of Dr. Rachel Ash, whom I have to thank for further progress notes:

Blood. Hemoglobin, 60 per cent; red blood cells, 3,296,000; leukocytes, 18,650, of which 75 per cent were polymorphonuclears.

Blood-pressure. Systolic, 105, diastolic: sounds loudly heard to zero.

Urine. Examination negative.

Two days after admission he was put on 20 minims. of tincture of digitalis three times a day. In a week this was increased to four times a day. The pulse record showed no slowing, in fact a slight increase in average rate after digitalis was started. He continued to run a low-grade septic temperature. A troublesome cough and signs of bronchitis developed. The intern's notes stated that the pulse had become irregular, but the type of irregularity was not recorded.

On July 30, about three weeks after admission, the notes say that "Marked dulness was noted over the left posterior chest and also marked impairment of resonance through the right posterior chest." He became very uncomfortable, though he did not complain of pain. The pulse was slow and irregular and became weaker. Friction rubs were heard over the entire chest. Heroin and morphin were given for the restlessness. A thoracentesis was done in the late afternoon and a few centimeters of blood withdrawn. He expectorated blood and died a few minutes afterward.

Clinical Diagnosis. Aortic stenosis and insufficiency, mitral stenosis, adhesive pericarditis.

Pathological Report. Autopsy No. A21, 137, Dr. W. A. Perkins.

The body was that of a very well-developed and nourished boy of eleven years, somewhat above the average in size. The general external examination was negative except for a few small hard nodules about each elbow. Of these one of a symmetrical pair

measured about ¾ cm. in diameter, and was situated over the posterior border of each ulna about 4 cm. from the tip of the elbow. The others were smaller and were situated over the apex of each internal condyle. All of the nodules were rounded, flattened and firmly fixed to the deeper soft tissues, but not to the bone. An attempt was made to dissect out one of the larger nodules through a small skin incision; as the dissection proceeded the nodule grew less and less distinct until no definite nodule could be made out. A bit of tissue, however, was removed from this region, including the subjacent periosteum and bone, and sections made for microscopic study.

The abdominal cavity was negative. The right pleural cavity contained about 200 cc of dark fluid blood and a small-sized clot, the latter lying between the base of the lung and the diaphragm; there were also several fibrous adhesions at the apex and base. The left pleural cavity was considerably encroached upon by a large heart; there were a few fibrous adhesions at the apex. The pericardial cavity was obliterated by dense fibrous adhesions.

Thymus. Rather large; tissue grossly negative.

Heart. Greatly enlarged, weight with adherent pericardium 1000 grams. The fused parietal and visceral pericardia formed a layer of varying thickness from 3 mm. over the left ventricle to 7 mm. over the right auricle, the two layers being readily distinguished and bound together by a third central thicker layer of translucent, edematous but tough connective tissue. Myocardium hypertrophied throughout and in the following ascending order: Right auricle, right ventricle, left auricle and left ventricle; the right ventricle measured 4.5 mm., the left ventricle 1 cm.; the tissue was rather pale brown, firm, tough and marked with a few small lighter colored depressed fibrous areas. Endocardium showed a slight, irregular, superficial fibrosis just below the aortic valve in the left ventricle. Heart cavities: there was a slight dilatation of the right auricle, a marked dilatation of the left ventricle, the latter encroaching upon the right ventricle. Valves: tricuspid valve-leaflets showed no thickening; the angle between the septal and infundibular cusps was bound down by what appeared to be short anomalous chordæ tendineæ; there was no evidence of any concomitant inflammatory process; the valve measured 10 cm.; Pulmonary valve appeared normal; measured 7.5 cm. Mitral valve showed a marked fairly uniform fibrous thickening of the leaflets, particularly of the anterior leaflet, with a shrinking up and disappearance from the latter of the accessory velum, resulting in the attachment of the chordæ directly on the free border of the cusp; this border appeared finely granular, rounded and somewhat thickened; neither mitral leaflet was much distorted, though there was a relative narrowing of the orifice; this measured 9.5 cm.; the chordæ in several instances, and particularly in the case of those

inserted into the anterior leaflet, were moderately thickened. Aortic valve: the cusps were all symmetrically and markedly thickened and retracted with, in addition, fibrous adhesions at the leaflet angles, the whole resulting in a narrowing and an insufficiency of the orifice. Coronary vessels possessed ample lumina no macroscopic sclerosis.

Aorta. The arch appeared moderately dilated, the intima smooth and normal.

Lungs. Right lung: pleural surface smooth except in region of adhesions about apex and base; upper lobe: pink gray in color with the posterior portions somewhat darker; on section the anterior portion of the lobe appeared slightly emphysematous, the posterior portion moderately congested, containing a slight excess of frothy blood-tinged fluid; mid-lobe emphysematous, external and cut surfaces gray, tissue dry, hypercrepitant; lower lobe on the external surface, at about mid-point, just lateral to the posterior border, is a small, roughly, quadrangular dark blue firm area about 1 x 1½ cm., marked by three small puncture wounds; section through this area showed continuation of the dark hemorrhagic discoloration into the lung tissue for a distance of 1½ cm. and ending in the region of a relatively large vein; the lower lobe otherwise resembled the upper but with the appearance of congestion somewhat more marked. Pulmonary vessels: negative; bronchus and branches contained a small amount of blood-tinged mucus; the bronchial branches of the middle lobe contained in addition two or three blood clots. Left lung considerably smaller than the right; pleural surface smooth except for apical adhesions; upper lobe showed a congested anterior portion and a slightly emphysematous posterior border; lower lobe, in addition to congestion, presented a moderate grade of atelectasis owing to compression from the enlarged heart; pulmonary vessels and bronchial branches same as on the right, except that the latter contained no blood clots.

Liver. Enlarged, estimated weight 2000 grams; upper surface roughened by adhesions and marked by a few small scattered seed-like nodules, the latter 1 mm. in diameter, with opaque yellow centers and pale translucent peripheries; cut surface of liver mottled dark red and brown, the lobules large and conspicuous, each with a large reddish center, and a brown periphery; tissue consistency normal.

Gall-bladder. Negative.

Spleen. Enlarged; estimated weight, 200 grams; surface roughened by fibrous adhesions; cut surface a mottled purple and dark red, the pulp soft, increased in amount; considerable scraping away on the knife, the connective-tissue elements conspicuous; the lymphoid elements less prominent; scattered over the cut surface were seen fairly numerous small, hard, calcareous, opaque orange-yellow nodules, similar to those in the liver capsule.

Gastrointestinal Tract. Appeared negative.

Pancreas. Firm; on section there appeared to be a moderate increase in the interlobular connective tissue.

Adrenals. Appeared normal.

Kidneys. About normal size; estimated combined weight 250 grams; right kidney: capsule stripped smoothly leaving a rather dark red lobulated surface; cut surface showed normal markings; cortex, 5 mm. thick; glomeruli present as red points; medulla normal; pelvis negative. Left kidney resembled right.

Bladder. Prostate, testes and epididymes not examined.

Culture from heart's blood was negative.

Thymus. Negative.

Heart. Pericardium: the three layers as described in the gross were readily distinguished, an outer layer of dense hyaline connective tissue, covered superficially with a less dense vascular fatty tissue (the parietal pericardium), an inner layer of areolar connective tissue containing fairly numerous scattered strands of compact hyaline connective tissue and a large number of small injected bloodvessels (the visceral pericardium) and a central layer of edematous granulation tissue containing occasional small, irregular masses of fibrin. All these layers were infiltrated with leukocytes, the inner and central layers particularly. Lymphocytes and plasma cells predominated, though in the central layer polymorphonuclear leukocytes became fairly numerous, while occasionally associated with the fibrin masses were seen large endothelial-like cells with one and sometimes two or three large vesicular nuclei. The cellular exudate extended sparsely into the stroma of the subjacent myocardium. Myocardium: the muscle fibers were generally thickened and hypertrophied and for the most part well preserved; in many places, however, and particularly in the region of the small vessels, fragments only of muscle fibers remained, the rest having been replaced by connective tissue. These replacement scars were comparatively small and irregularly diffuse in their distribution. Furthermore, throughout they showed a moderately extensive infiltration with lymphocytes, plasma cells, eosinophiles, a few polymorphonuclear leukocytes and fairly numerous endothelioid cells. The last named were relatively large, round, oval or more or less elongated cells with abundant cytoplasm and large vesicular nuclei; most of them contained one nucleus; several, however, contained more than one, often appearing as actual giant cells. These endothelioid cells occurred usually in groups and near small bloodvessels, thus forming the so-called Aschoff bodies. (See microphotographs herewith.) The latter are so characteristically present in acute rheumatism involving the heart that the process is called by some rheumatic carditis. The accompanying illustrations show two such bodies, one composed of mononuclear endothelioid cells, the other containing some giant forms as well, and both typically situated in the neighborhood of

small bloodvessels. Several of the vessels showed an irregular thickening of the intima, with encroachment on their lumina; there were no thrombi.

Heart Valves. A section through one of the segments of the mitral valve showed this composed of a fairly dense connective tissue in which were seen small bloodvessels that extended well out almost to the free edge of the cusp. There were also present several moderately sized elongated mononuclear cells arranged in a narrow zone near the ventricular surface of the valve while along the auricular surface were seen in one or two places scattered lymphocytes. At the attached border of the cusp there was a fairly abundant infiltration with lymphocytes and larger mononuclear cells and occasional polymorphonuclear leukocytes occurring chiefly as small perivascular foci. A similar cellular infiltration was present in the adjacent myocardium and endocardium. In addition, Aschoff bodies were seen in the myocardium, while a suggestion of such bodies was noted in several places in the endocardium. A second section through another region of the mitral valve showed an inflammatory process similar to the above except that the reaction appeared more acute, as evidenced by the presence of a larger number of polymorphonuclear leukocytes.

The lungs presented the picture of chronic passive congestion with injected tortuous capillaries and alveoli partly filled with serum and moderate numbers of heart failure cells. In addition certain areas showed a slight grade of atelectasis, others a definite emphysema. A section through the lower lobe of the right lung in the region of the puncture wounds mentioned in the gross description showed a marked hemorrhage into all the alveoli, while in the center of this hemorrhagic area several fairly large vessels were noted engorged with blood.

Liver. The central veins and the sinusoids, except those immediately surrounding the portal spaces, were congested, the liver trabeculæ compressed, the portal spaces themselves infiltrated with lymphocytes and a few plasma cells. Section through one of the seed-like nodules in the capsule mentioned in the gross showed concentrically arranged hyaline connective tissue with a softened necrotic center.

Spleen. There was a diffuse increase in connective tissue; the pulp contained an excess of red blood cells, while an occasional nodule similar to that in the liver capsule was found outlined by a band of hyaline connective tissue, but with a relatively large center composed of amorphous material and containing some lime salts. These nodules occurred singly or in groups of two or three. Associated with them was a slight inflammatory reaction consisting of lymphocytes and a rare giant cell, the latter with peripherally arranged nuclei. The process in both liver and spleen probably represents the end result of a previous tuberculous infection.

Pancreas. The vessels were congested, the interstitial connective tissue infiltrated with a moderate amount of hemorrhage, probably artefact.

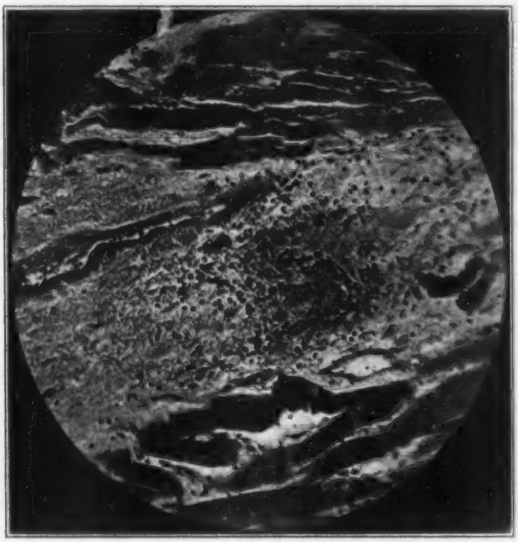

FIG. 3.—Aschoff bodies.

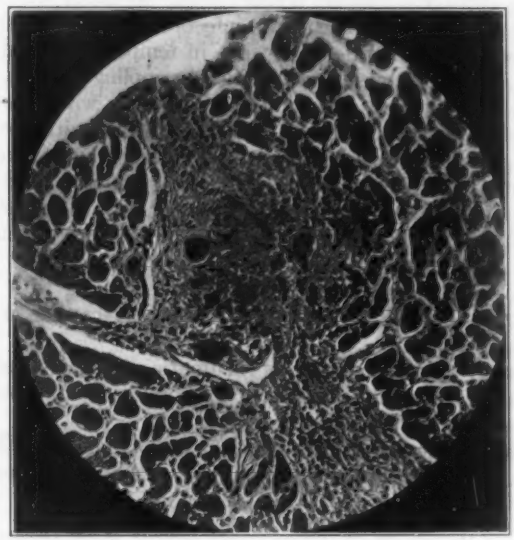

FIG. 4.—Aschoff bodies.

Kidneys. The tubular epithelium showed cloudy swelling; most of the tubules contained a finely granular albuminous material; the vessels were injected; the glomeruli generally were large.

Lymph Node. Congested.

Subcutaneous nodules: sections were negative, showing only normal bone, periosteum and striated muscle. In view of these findings, it is suggested that such nodules be removed "en bloc" without attempted dissection.

PATHOLOGICAL DIAGNOSIS. Subcutaneous rheumatic nodules about elbows; marked subacute and chronic fibrous obliterative pericarditis; diffuse fibrous myocarditis (rheumatic type); chronic mitral and aortic endocarditis, with stenosis and insufficiency; congenital adhesions at the septo-infundibular angle of the tricuspid valve; marked myocardial hypertrophy, especially of the left ventricle; marked dilatation of the left ventricle; general chronic passive congestion; fibrosis of spleen; parenchymatous degeneration of the viscera; multiple miliary calcareous nodules in liver and spleen; bilateral fibrous pleural adhesions; puncture wounds in lower lobe of right lung, with right hemothorax.

Discussion. The presence of a few isolated nodules which disappear with the subsidence of arthritic and cardiac symptoms may or may not be of great significance. Our personal experience is not prolonged sufficiently to pass judgment. We can say, however, that all cases which, while under observation, have had recurring crops of nodules have shown serious and progressive cardiac damage. Fibroid nodules seem to occur frequently in that subacute type of rheumatic infection in which an apparently mild carditis, with little if any rise in temperature, and with no severe joint symptoms, develops into a crippling stenosis, damaged muscle or adherent pericardium. The case with acute onset, high fever, red, swollen joints and rapid heart, with the murmur of regurgitation which responds to treatment and makes a good recovery, remaining without rheumatic symptoms until another similar acute attack occurs, much more rarely shows nodules.

We believe that recurring rheumatic nodules are of more prognostic value than any other one sign in rheumatism. They are our most significant warning that we are dealing with a serious infection which will probably result in great cardiac inefficiency if not in death.*

Summary. In 38 instances of rheumatic cycle cases seen between September, 1919, and September, 1921, fibroid subcutaneous nodules were present in 17, or 44.7 per cent.

Of those patients having nodules, 6, or 35.9 per cent, died during this period. In only one instance did death occur in a patient not having nodules.

* We feel that we owe an apology to such pioneers as Sir Thomas Barlow for attempting to draw conclusions from the study of a rather small selected group of cases observed during the brief period of two years.

Of the 38 cases, 17 were grouped as having serious cardiac damage. Of these 17, 13, or 76.5 per cent, had nodules.

Our series of cases probably includes an abnormally large proportion of a severe type of infection, and should not be judged as entirely representative of the usual incidence of nodules in this part of the world.*

LINITIS PLASTICA—WITH REPORT OF TWO CASES.

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The term linitis plastica was first used by Lewis Brinton in 1854 to describe a diffuse or circumscribed increase in the connective tissue of the stomach, involving chiefly the submucosa, and, to a lesser degree, the other layers, with marked thickening of the walls of the stomach, a diminution (rarely an increase) in the size of its lumen, and characterized by an insidious onset, a slowly progressive cachexia, and a fatal termination.* Fully twenty-two other terms have been used to describe this condition, the most suggestive of which are: leather bottle stomach, chronic interstitial gastritis, cirrhosis of the stomach, fibroid induration of the stomach and chronic stenosing gastritis.

Although this condition of the stomach had occasionally been described in medical literature before Brinton's time, namely by Lieutand in 1779, by Andral and Cruveilheir in 1829, and more frequently by other writers after 1829, the credit for recognizing and naming it as a separate disease belongs to Brinton. The most exhaustive study of this disease since Brinton's time was probably that made by H. M. Lyle in 1911, when he described 131 cases gathered from literature, and added 1 case of his own. Since this time not more than a dozen cases have been reported.

Pathology. There has been considerable difference of opinion regarding the classification of cases of linitis plastica. Diffuse carcinoma of the gastric wall produces a condition which is almost identical with the benign type, and some authorities claim that all cases are malignant. Others claim that only the benign cases can rightly be called linitis plastica. Most writers now agree, however, that to both the benign and malignant types the term linitis plastica may properly be applied, Lyle's study, mentioned above, being based on a total of 114 carefully studied cases, of

* We have to thank Dr. William Palmer Lucas, Dr. Florence Holsclaw, Dr. Rachel L. Ash and Dr. Langley Porter for allowing us to study past histories and for inviting us to follow many of the rheumatic cycle cases on their services.

which 62 were benign and 52 malignant. The benign cases of this disease may be of two types, the localized and the generalized. The former type, occurring in the form of small placques, is rare. In the generalized type, except in the rare instances where there is a dilatation as a result of pyloric stenosis, the stomach is found to be hard, rigid and contracted, with thickened and inelastic walls, stomachs as small as 4 inches long, by 2 inches wide, and walls 1 inch thick, with a capacity of not more than 4 ounces, having been reported. The normal stomach is 12 by 5 inches, the wall $\frac{1}{5}$-inch thick, and capacity 40 ounces.

The thickening of the walls usually commences at the pylorus, and spreads toward the cardia. It does not, as a rule, involve the duodenum, but may involve the esophagus. The tissues are grayish in color and there is often an associated adhesive peritonitis. Analogous lesions may be found in the large or small intestines.

Microscopically, the connective tissue of the submucosa is found to be hypertrophied, often causing atrophic, inflammatory or cystic changes in the mucosa. The submucosa shows an interlacing endarteritis, this, with the connective tissue change, producing the weave-like, interlacing effect from the appearance of which the name linitis was coined.

Nests of epithelial cells, possibly portions of gastric glands or mucosa which have become isolated, occur in the submucosa. These closely resemble carcinomatous areas, and may frequently have led to confusion in diagnosis. The connective tissue hypertrophy extends through the muscular coats, causing atrophy of the muscular fibers, and infiltrates the subserosa. The neighboring lymph glands show a fibrosis. In the malignant cases the lesion is an interstitial carcinomatosis, the gross effect being the same as in the benign cases. Gastric syphilis may also occur in the same form.

Etiology. Linitis plastica is a disease occurring in persons of carcinoma age, nearly all cases reported being between the ages of forty and sixty. It affects males twice as frequently as females. Usually there is a history of some previous condition which may have some etiological significance, such as cardiovascular disease, alcoholism, gastric ulcer, syphilis, tuberculosis or occupational trauma.

Symptoms. These are not characteristic, there being a gradually increasing train of dyspeptic symptoms, with anorexia, nausea, upper abdominal discomfort or pain, vomiting attacks, alternate constipation and diarrhea, and a more or less marked secondary anemia—in short, the general symptoms are those of the achylia gastrica which is usually present. Vomiting of blood rarely occurs. A symptom which is very suggestive, being a direct result of the actual diminution in size of the stomach and the inelasticity of its walls, is the feeling of fulness after the ingestion of even very

small quantities of food, and the vomiting or regurgitation of any excess above a certain amount; the small quantities may, however, be very frequently repeated without discomfort, due to the rapid emptying of the stomach. Ascites may develop later. The duration of the symptoms before a patient seeks medical advice may vary from a month to a couple of years, during which there has occurred progressive anæmia and loss of weight and strength.

DIAGNOSIS. The only symptom which is of aid in the diagnosis is that due to the small capacity of the stomach, mentioned above. In advanced cases a sausage-like tumor may be felt lying transversely in the epigastrium. On inflating the stomach, or injecting water into it through a tube, the air or water may be felt gurgling rapidly through this mass. Even where there is no mass to be felt, the rapid transverse passage of the air or water into the duodenum can often be made out, and is of diagnostic value.

The test-meal examination shows the rapid emptying of the stomach and the absence or reduction of the hydrochloric acid. Lactic acid is present only in the rare cases where dilatation and consequent stasis have occurred. Fluoroscopical examination shows the small size stomach, with marked hypermotility, the barium mixture passing rapidly across the upper abdomen and filling the intestinal coils. Roentgenography will show the small tube-like stomach, its walls rigid, and with no evidence of peristaltic waves.

Although the diagnosis has been rather rarely made before operation or autopsy, the above findings, in a patient of middle age, may justify a presumptive diagnosis of linitis plastica. Whether the condition is benign or malignant can only be determined by microscopical examination, and is of no great importance in the treatment, this being the same in both types.

Linitis plastica must be differentiated from a movable kidney or spleen, pyloric carcinoma or ulcer, pyloric syphilis, malignancy or excessive mobility of the transverse colon, chronic adhesive or tuberculous peritonitis, and portal cirrhosis.

The *prognosis* is not good. The condition is progressive, and even with the removal of the gastric focus there may be progressive changes in the foci in the colon, rectum or small intestine, causing stenosis. The average length of life for the benign cases is four years, for the malignant cases, two years.

The *treatment* is operative. A gastrectomy should be performed, either primarily, or, in advanced cases, after a primary jejunostomy has permitted the patient's nutrition to be improved sufficiently by jejunal feeding, to render him operable.

As a preliminary to operation, where the pylorus is sufficiently patent to permit the passage of a tube, duodenal feeding is indicated. If the tube will not pass, the gastric motor efficiency still remaining should be tested out by injecting into the stomach, through a Rehfuss gastric tube, measured amounts of fluid until

the stomach is filled, and then aspirating the fluid remaining after a definite interval, to see the amount the stomach has evacuated during that period of time. The exact amount and frequency of feedings can thus be determined, and concentrated liquid nourishment can thus be given. In the writer's first case, described below, 1½ ounces of a concentrated solution of dextrose, peptones, alcohol and fats was given through the tube or by mouth every fifteen minutes, and easily taken care of by the patient, so that by this method, combined with rectal feeding, 100 to 150 ounces of liquid, containing over 2500 calories was administered every twenty-four hours for several days, until the patient was considered to be in operable condition.

Case I.—A. H., female, aged thirty-eight years, a housewife, married ten years, denied venereal infection, but admitted a few self-induced abortions. She had been in the "show business" for years, and had been more or less addicted to alcohol and late suppers. Except for malarial fever sixteen years before, she had always been healthy, and weighed 180 pounds when, in 1911, at the age of thirty-five, she had an attack of pain, vomiting and jaundice, called gall stones by her physician. After that she had had occasional slight digestive disturbances. She was first seen by me at the Brooklyn Hospital in the early part of 1914, when she was suffering from epigastric pains immediately after eating, going through to the back, vomiting forty minutes after eating, sour regurgitation, constipation, and loss of weight, which symptoms had been persistent for about six months. Examination showed a moderate pyorrhea; head and chest were negative. The abdomen was flabby, distended with gas, and tender in the epigastrium and to the right. No masses were discernible. Pelvic examination was negative. Rectal examination showed an anal fissure and a rectal polyp. The systolic blood-pressure was 105, the diastolic 70. The blood showed a secondary anemia and a negative Wassermann reaction. Repeated test-meals showed a total achylia, with marked hypermotility. The string test was negative. There was no occult blood in the stools. The urine contained an excess of indican. Fluoroscopy showed the stomach small, slightly ptosed, with a very small fundus and a narrow tube-like passage continuous with the duodenum, through which the barium passed with great rapidity, although no peristaltic waves were visible. One hour after the examination the patient took tea and crackers, which were vomited, but no barium was present in the vomitus, showing the rapid emptying of the stomach. The patient at this time was weighing about 100 pounds, being 80 pounds underweight. A provisional diagnosis of hyperperistalsis, due to some reflex irritation, was made, but the possibility of a linitis plastica being present, mentioned. The rectal polyp was removed, to exclude this as a

reflex cause, but no relief resulted. On July 1, 1914, Dr. John H. Long performed an exploratory laparotomy. The stomach was found to be somewhat smaller than normal, with greatly hypertrophied walls, thought to be due to hyperperistalsis resulting from the pylorus being bound to the gall-bladder with dense adhesions. The adhesions were freed, but the gall-bladder, being found hard, but patent, was left in. The interior of the stomach was explored through an incision in its anterior wall, but nothing was found. The appendix was removed. The patient improved markedly after this operation, but weighed only 89 pounds on her discharge from the hospital.

In the next six months she gained 25 pounds, and some hydrochloric acid began to appear in the stomach contents. Then she began again to have epigastric pain, vomiting and loss of weight, dropping to 91 pounds in November, 1915. She continued to get worse, and was lost track of until May, 1916, during which time she had been abandoned as an inoperable carcinoma case and reduced to a moribund condition. She was retching and vomiting constantly, urinating a few ounces at a time every twenty-four to forty-eight hours, and having a bowel movement once in ten days, when next seen by me. No mass could be palpated, although emaciation was the most extreme the writer had ever seen. With a duodenal tube in the stomach, it was found that but 1 ounce of fluid could be injected into that organ at one time, any excess being regurgitated through or alongside the tube. This amount of fluid was gone from the stomach, however, in fifteen minutes on repeated tests. The fluid removed from the stomach was anacidic and contained a little occult blood. The tube would not enter the duodenum. Inflation through the tube disclosed the slight distention at the point of the 1 ounce cavity, and then a rapid bubbling of the air across the epigastrium, apparently to another larger cavity, to the right. A diagnosis of linitis plastica, with hour-glass constriction due to scar formation at the point of the gastrotomy, was then made. The patient was too weak for roentgenography. She was fed 1 ounce of a solution of dextrose, peptones and alcohol every fifteen minutes, and as much dextrose solution per rectum as could be retained. She thus received 2500 calories or more per diem for nearly three weeks during which time the capacity of the stomach was increased to 1½ ounces, Dr. Long at this time considering conditions sufficiently improved to warrant the slight amount of shock occasioned by the procedure, did a duodenostomy under local anesthesia, the patient receiving a hypodermocylsis during the operation. He expected to do a gastrectomy later, but the patient died suddenly twenty-four hours after the operation, apparently from uremia.

The principal abnormal findings at autopsy were as follows: The stomach was found buried in adhesions to the liver, gall-

bladder, pancreas and abdominal wall. On freeing it, the stomach was found to measure 5 inches in length from cardia to pylorus and 2½ inches in width. The fundus had a capacity of 1½ ounces, and about 2 inches from the cardia the stomach became narrow, with a tough wall ½ inch thick and deep rugæ, this excessively thickened area corresponding to the gastrotomy scar (Fig. 1). The pylorus was fibrous and hard. A finger introduced into the cardia revealed an obstruction at 2 inches, which permitted only a match to pass through it. The microscopical findings were typical of those described for the benign type of linitis plastica. The duodenum was found adherent to the gall-bladder and pancreas, but was otherwise normal. The terminal ileum was reduced to a

FIG. 1.—Stomach viewed from front. Thickness of wall shown where cut edge is everted. Capacity 1½ oz. Duodenostomy at lower right corner.

fibrous cord, but was patent. The colon was negative. The left ovary was cystic.

This case therefore presented the unusual condition of an hour-glass constriction occurring in the course of linitis plastica.

CASE II.—M. A., female, aged fifty-seven years, Irish, housewife, applied at the Long Island College Hospital for treatment November 20, 1921. She had been married thirty-six years had had seven children and four self-induced miscarriages. Her family history was negative. She had always been healthy except for some minor postpartum infections and an attack of mild arthritis as a young woman. The nervous symptoms of the menopause had been continuous since the cessation of menstruation at age of

fifty. She had never eaten much meat, but had indulged moderately in wine and whisky.

In June, 1921, the patient, after a short period of anorexia, had begun to have attacks of diarrhea, with loose watery stools after meals. There was also a pain in the epigastrium, and to the left, increased immediately by taking food or by lying on her back. For two weeks before admission there had been a very marked nausea and the regurgitation of all food taken above a certain moderate amount. There had been a steady loss of weight and strength.

Examination showed an emaciated, weak, pale woman, with all false teeth; infected, cryptic tonsils; normal heart and lungs and no glandular enlargements. Blood-pressure, systolic 122, diastolic 72. Her abdomen was not distended, and there was a sausage-like, hard mass about 1½ by 3 inches, lying transversely across the epigastrium. This mass was movable and not attached to the abdominal wall and was slightly tender on firm pressure. The appendix region was also tender. Pelvic examination showed a lacerated cervic and an old parametritis. There were no other abnormal physical findings.

Laboratory findings were as follows:

Urinalysis and renal function tests negative.

Gastric analysis by fractional method showed a true achylia gastrica with blood present in all specimens removed.

Blood count showed a moderate anemia and the Wassermann reaction was negative. Blood chemistry was normal.

Roentgenological examination showed on fluoroscopy a stomach constricted in its middle portion for about 3 inches, with cardiac and pyloric ends and duodenum somewhat dilated, the barium meal passing rapidly through the constricted area. The roentgenograms showed this deformity with the outline of the constricted area perfectly smooth (Fig. 2). The stomach emptied rapidly and the colon was negative except for some retention of barium in the appendix after forty-eight hours.

Operation, November 16, 1921, by Dr. Emil Goetsch, under local anesthesia, showed at once several large omental glands along greater curvature of stomach, one of which on removal showed carcinomatous changes. The entire stomach, with the exception of slightly dilated portions at the cardia and pylorus, was one large hard mass and there were numerous glands palpable in the omentum, although no liver metastases were found. The abdomen was closed without further procedures.

Following operation, the patient continued to vomit, and a month later began to have gastric hemorrhages every few days. Only small amounts of liquid could be taken at one time and the patient was merely sustained by the use of morphin and alcohol. She died February 16, 1922, three months after operation.

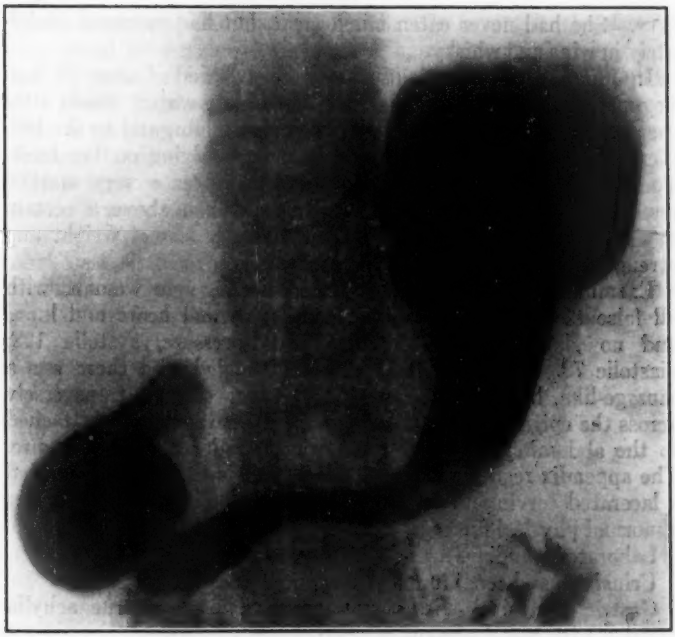

FIG. 2.—Roentgenograph of stomach immediately after barium meal. Pouches of cardia and pyloric antrum, with constricted area.

FIG. 3.—Stomach viewed from back. Everted cut edge shows thickness of wall. Dark area in mucosa is vascular, superficial ulcer which caused hemorrhages. Capacity 3 oz.

Autopsy (by Dr. A. Murray): The only abnormal findings besides those in the stomach were a brown atrophy of the heart and a chronic passive congestion of the liver and signs of senile

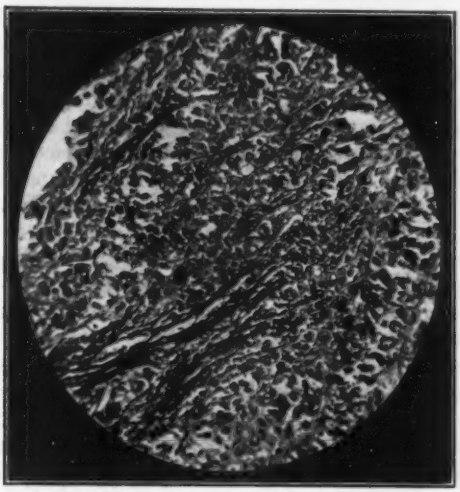

FIG. 4.—Microscopic Section of the Stomach. Low power.

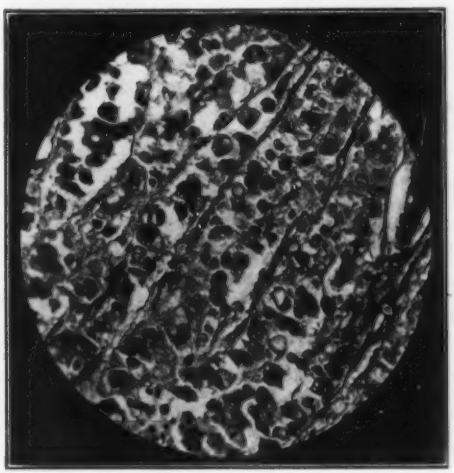

FIG. 5.—Microscopic Section of the Stomach. High power.

atheroma of the aorta. The esophagus was normal. The stomach was 20 cm. long and 8 cm. in diameter and had a normal outline (Fig. 3). Its walls were uniformly infiltrated and made dense by

what appeared to be carcinoma. The surface was covered by pearly white nodules loosely adherent to surrounding structures. The mucosa at the cardia was congested and apparently hemorrhagic. A large ill-defined ulcer covered with foul necrotic slough was present on the middle portion of the anterior wall. The distal 3 cm. of the stomach, the duodenum and the rest of the alimentary tract appeared normal. The root of the omentum was densely infiltrated with new growth, as were the retroperitoneal lymph nodes along their entire length. The abdominal aorta was large and replaced by tumor. Microscopical examination of the stomach (Figs. 4 and 5): All layers were uniformly and completely invaded by carcinoma so that only traces of the original structure remained. Nerves, bloodvessels and the islands of the muscularis mucosæ were left intact. The epitheleum was wanting from the mucosa and there were few lymphoid nodules in the submucosa. In the muscular wall, cords of tumor cells had entirely replaced muscle bundles, but had followed their course, so that the tumor cords had the arrangement of the original muscle bundles.

The carcinoma was of the medullary type, with few distinct foci which were composed of columnar epithelial cells.

The heart showed brown atrophy, the liver, passive congestion, and the kidneys were arteriosclerotic.

Diagnosis. Carcinoma of the stomach, linitis plastica.

Summary. Two cases of linitis plastica, confirmed by autopsy, are reported.

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ACUTE PERFORATIONS OF STOMACH AND DUODENUM (WITH A REPORT OF SIXTY CASES).*

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A study of the results of operations for perforations of the stomach and duodenum shows very conclusively the value of prompt recognition and relief of this condition.

The 60 cases reported have been treated on the First Surgical Division of the New York Hospital from February 1, 1913 to April 30, 1922. The operators have been Drs. Gibson, Lee, Hitzrot and Farr. Fourteen of these cases were reported by me[1] in a paper published in 1916, and some of these cases were also reported in a paper by Dr. Farr[2] 1920.

The opinions expressed represent my personal views based on my experience since 1907 when I did my first operation for this condition.

The results obtained in this series confirm my previous belief of the desirability of aiming simply to close the perforation, leaving remote and problematical after results to be taken care of as necessity arises.

The mortality of the whole series, 16.6 per cent (Table I) is not high.

TABLE I.—MORTALITY RATE.

Cases.	Perforations.	Deaths.	Per cent.
43 }	12 hours }	3	6.6 (2.3)
2 }	18 " }		
5	24 "	1	20
10	Over 24 hours	6	60

It is particularly gratifying to note the small per cent, 6.6, in the first eighteen hours, only 3 out of 45 patients succumbing. In fact, the mortality really should be estimated as 2.3 per cent as 2 out of these 3 deaths occurred under conditions which would be thrown out by many writers in reporting their results. The relative benignity when recognized and operated early becomes evident.

Case 210312, male, aged fifty-eight years, gave a gastric history of twenty years duration; perforation of ten hours; showed marked collapse with cyanosis and weak irregular pulse and subnormal temperature on admission; rallied under morphin and operated on under gas-oxygen. The night after operation the patient got out of bed, walked across the ward, drank a glass of cold water and

* Read before the meeting of the American Surgical Association in Washington, May 2, 1922.

[1] Surg., Gynec. and Obst., April, 1916, p. 388.

[2] Ann. Surg., November, 1920.

collapsed. The temperature went to 105° F. and pulmonary edema developed. Death occurred a few hours later (autopsy).

Patient 220548 died forty-five days after operation, twenty-three days after an operation for empyema which could not be demonstrated to follow in any way the results of the first operation.

As will be pointed out later, I have never been in favor of performing a gastroenterostomy as a routine operation, although admitting its occasional necessity, and the low mortality of these early cases strengthens this belief and a study of the late results is also very satisfactory.

The particular points of interest in such a study will be to note: (1) Basis for early diagnosis. (2) Technical procedures, particularly in reference to the performance of gastroenterostomy. (3) After results and particularly bad results requiring further operative measures.

In regard to diagnosis we note in Table II, that the bulk of patients give a previous history of gastric disturbance, most of them of long standing.

TABLE II.—PREVIOUS GASTRIC DISTURBANCE.

	Gastric.	Duodenal.
No previous trouble	9	5
Trouble dating back less than a year	9	3
Trouble of long standing	9	21
Too ill to obtain a history	1	1
One previous attack five years ago, none since	0	1
Time indefinite, slight indigestion at times	0	1
	28	32

We note also that the onset is universally acute and that in all cases pain is given as the chief complaint, usually described as "knife-like." The symptoms in a typical case are unmistakable. Pain "in the pit of the stomach" comes on usually without premonition, is agonizing and often followed by considerable shock. Rather less than half of the patients vomit but vomiting has always been secondary to the pain. The vomitus rarely contains blood.

The patient becomes cold, sweats, and the facial expression reflects the great agony. Soon after these initial symptoms there comes probably quite often a symptom which is seldom described and seldom elicited because of its temporary duration and after it has disappeared the patient forgets about it as his attention is concentrated on the persisting abdominal pain. I refer to severe pain coming on within a few minutes of the perforation and felt in the supraclavicular fossa, usually the left. It lasts only a few minutes, seldom more than fifteen. Given a clear history of this pain with a sudden onset I feel there is no symptom that is more characteristic.

The next most marked feature is a retraction of the abdomen,

board like rigidity of the upper half, and great tenderness to pressure. At this stage there are practically no other symptoms worthy of consideration. Much time is wasted by some practitioners at this stage on three perfectly worthless diagnostic features (1) temperature, which may be low, may be normal, or may be slightly increased; (2) changes in the white cell count of the blood, total leukocytosis, percentage of polynuclears and their relation to each other. These changes will not take place until later; (3) obliteration of the liver dulness, a beautiful theoretical symptom which I have never been able to demonstrate in any perforation of the gastro-intestinal tract from any cause and never expect to.

With the progress of the condition we have a sequence of symptoms which are those of a peritonitis. If a patient is seen twenty-four hours after the perforation and a clear history has not been obtained of the previous condition and of the initial symptoms, attention is frequently centered on the possibility of a peritonitis from a perforation of the appendix, and this possibility is emphasized by the mechanical gravitation of the exudate from the upper part of the abdomen down the right gutter, giving tenderness most intense over the right lower quadrant.

The above classical picture is not infrequently modified, symptoms being milder and the onset less clear cut. The alteration of symptoms probably depends a good deal on the physical conditions, being less in a minute perforation with a minimum of extravasation of gastric contents. Moreover, some of these minute perforations become plugged by omentum, greatly modifying the course of the condition.

The conditions which may simulate an acute perforation of the late type are those of an intra-abdominal lesion which would call for interference, particularly appendicitis, acute cholecystitis, acute pancreatitis, and acute bleeding of a gastro-duodenal ulcer. It must also be remembered that occasionally two acute abdominal conditions occur simultaneously. All the conditions just described would justify opening the abdomen even on a mistaken diagnosis as a chance is given to remedy an acute and often dangerous condition.

The most serious mistake and one which I have once personally committed is operating in the face of an impending pneumonia as the signs are often quite identical, the pulmonary physical signs being delayed in their onset and the history misleading. A sign which I have never seen described and have only lately thought of trying is auscultation over the pyloric region with the possibility of recognizing the to and fro passage of air from the stomach into the peritoneal cavity.

Diagnosis of the Condition When the Abdomen is Opened. When operating for a possible perforation or for any acute abdominal lesion that is obscure, I recommend the employment of a procedure

which has been of great value to me for many years, namely opening the peritoneum under water. An incision is made down to the peritoneum which is seized between two clamps; the abdominal wound is flooded with water and peritoneum opened. Even the escape of a single bubble of air shows necessarily that there must be a communication with the gastro-intestinal tract.

On the other hand, there may be little or no air in the cavity and the perforation may be temporarily sealed off.

If there is any appreciable amount of fluid in the peritoneal cavity one is usually impressed with the oily or vaseline like character, sour smell, or possibly recognition of food particles, bile or other stomach contents. The administration of a teaspoonful of weak methylene blue solution by mouth just prior to giving the anesthetic is also of value as the stomach contents are easily stained by it.

Anesthesia. Anesthesia is that of the surgeon's choice. Personally I favor open ether, drop method, over all other forms.

Incision. The lesion being in the great majority of cases juxta pyloric, the incision is placed in the upper epigastrium to the right of midline. This should be a large incision, allowing of easy access to the perforation.

Operative Procedure. The perforation having been located usually with the greatest ease, the first thing in order is to close it. This statement may seem unnecessary but I have seen a lot of time wasted in sponging out the abdomen and puttering around while the hole is still discharging gastro-intestinal contents. Some operators report difficulty in closing these perforations; but so far I have been able always to close them securely, usually with mattress sutures or purse-string sutures of catgut. I occasionally feel more secure by fixing the sutured surface with some structure such as omentum or gall-bladder.

While these procedures have been under way, the assistant should have evacuated the abdomen of the extravasated contents. My own feeling is that with rare exceptions, and perhaps only in the later cases, is a drain necessary or even useful.

Cultures. A culture should always be taken and it will be surprising how often an extensive and muddy looking exudate will fail to show a growth.

Dr. E. G. Alexander, of Philadelphia, tells me that he has never obtained a growth within the first eighteen hours.

Closure of Wound. Closure of the wound should be done with much care and accuracy as these wounds do not heal very well and show a tendency to break open.

After-care. I think it extremely important to feed the patient at an early date and push nourishment rather more freely than is the custom.

Gastroenterostomy. In 1916[3] I gave in detail my reasons for not advising the performance of gastroenterostomy as a routine measure. I have had no reason to change my views and the results of the cases here reported, both immediate and remote, justify the belief. Of the 4 gastroenterostomies performed in this series a satisfactory suture was not or could not be made in three of them.

Briefly stated my arguments against routine gastroenterostomy are:

1. It prolongs and complicates what is usually a simple, quick and safe operation.

2. It is only very rarely needed as a technical adjuvant to correct or forestall a stenosis.

3. Few patients have any further trouble with their stomachs after recovery from acute perforation. Moreover, a gastroenterostomy is not a cure all or sure preventative for ulcers, acute or chronic.

4. Gastroenterostomy is an operation which has a certain proportion of recognized drawbacks and dangers.

5. What seems to me the most serious objection is the authority and teaching of particularly successful operators in influencing the unskilled or inexperienced surgeon to do more than he should normally try to accomplish.

End-results. At time of discharge all patients were free of symptoms with the exception of 2 cases that had a little distress after eating; but three months later were entirely well. All patients were reëxamined or reports obtained at variable periods and always three months after operation.* So far the results have been as follows:

Entirely free from symptoms, excellent result	37
Recurrence of symptoms	8
No data	4

Reoperation. We were obliged to reoperate in 16 per cent of our patients. The details are given as they present much of interest.

1. Case 215651. Patient well for eight months. Symptoms then returned. Lost twenty pounds. At operation (two years after first operation), tight constriction of the pylorus found. Moderate amount of thickening on each side but no definite induration or ulcer. Posterior gastroenterostomy. Four months later in excellent health. Gained twenty-three pounds.

[3] Loc. cit.

* Our thanks are due to Dr. Arthur L. Holland, Associate Physician of the New York Hospital for his energy and devotion in investigating the condition of our patients showing poor end-results, particularly by making very accurate fluoroscopic examinations and for his wise counsel in directing the most important after-treatment in all cases.

2. Case 216941. Patient free from symptoms for two years. At operation (two years and one month after first operation) marked duodenal ulcer on superior-posterior surface of duodenum, size of thumb. Pylorus moderately stenosed. Duodenum dilated. Cause adherent gall-bladder. Polya-Mayo resection of pylorus. One year later in excellent health and gained a great deal of weight.

3. Case 202624. Patient perfectly well for five and a half years. Came in for operation three weeks after onset of symptoms. At operation ulcer of duodenum well away from the pylorus, size second phalanx of thumb, very hard and irregular. Wound broke open on second postoperative day. Resutured, but on the twelfth postoperative day again broke open. Did not do well at any time. Vomited and ran constant temperature. Looked the picture of acidosis although urine was negative. Death resulted on twenty-seventh postoperative day.

4. Case 221456. Patient not well since discharge from hospital. Complaints, epigastric pain, loss of appetite, constipation. At operation four months later diffuse adhesions to omentum. Tight stenosis of pylorus due to cicatrization of old ulcer. Posterior no loop gastroenterostomy. Five months later much improved.

5. Case 215114. Return of symptoms one year after operation. Patient came in for operation three months after onset of symptoms. At operation diffuse adhesions, particularly of gall-bladder to duodenum, and of distal section of stomach to abdominal wall. All these were separated. First part of duodenum seat of hard callous ulcer, causing marked stenosis. Posterior no loop gastroenterostomy. Roentgen-ray diagnosis of pulmonary tuberculosis. Never proven from sputum. Died a year after discharge, apparently from pulmonary tuberculosis.

6. Case 229779. Patient readmitted eleven months after first operation. Duodenum is the site of an apparently healed perforation imbedded in solid mass of scar tissue and producing considerable stenosis. On account of technical difficulties thought wisest to do only a gastroenterostomy. Five months after discharge patient in good health and gained weight.

7. Case 232506. Patient readmitted six months after first operation. Numerous adhesions, particularly of gall-bladder to stomach. Stomach is folded over on itself by large adhesion. Ulcer $\frac{3}{4}$ x $\frac{3}{8}$ inch situated on posterior-superior wall. Pylorus turned away from duodenum. In view of mildness of symptoms referable to ulcer decided to do a gastroenterostomy. Five months later condition somewhat improved although still has pain and has been told he has another ulcer. Has been living on a very limited diet. Gained a little weight.

8. Case 207098. Gastric history of long standing. Perforation four and a half years ago—suture. Patient free from symptoms

until six weeks prior to present admission. Then had attack of epigastric pain. Suturing of perforation, two hours old. Perforation occurred in exactly same location as former one, to the duodenal side of the pyloric vein on the anterior aspect. Two years later in excellent health.

Two facts may be noted; that we have a large proportion of saved cases as possible candidates for trouble and if we had performed an "optional' gastroenterostomy on all our patients it is quite probable that 16 per cent or more would have reported more or less serious gastric disturbances.

Two of these cases requiring operation were originally long delayed cases and might have succumbed to a prolonged operation if a gastroenterostomy had been performed.

The conditions found in the 8 reoperated patients were:

5—Stenosis of pylorus.

1—Stenosis of duodenum by cholecystitis.

1—Adhesions.

1—Reperforation.

This gives a 10 per cent sequence of stenosis of pylorus.

Of the cases requiring reoperation the ulcers, with one exception, were situated in the duodenum. Of the results after operation 5 are good, 1 patient is having mild but rather persistent symptoms, 1 patient died and 1 patient died a year later of pulmonary tuberculosis.

The operations performed were gastroenterostomy (5); Polya-Mayo resection (2); suture of acute perforation (1).

We have operated on every patient in whom a possible diagnosis of acute perforation could be entertained. We had 1 case of perforated gastric ulcer revealed at autopsy. The patient was brought in in moribund condition, unconscious, without any history and died one and a half hours after admission.

Additional Data. 1. Location of ulcer.

Gastric, 28; deaths, 6 (1 ten hours; 5 over eighteen hours) 21 per cent.

Duodenal, 32; deaths, 4 (2 ten hours; 2 forty-eight hours) 12 per cent.

2. Sex:

Male, 56.

Female, 4 (3 gastric).

3. Age:

No patient under twenty.

Greatest number between thirty and forty.

4. Operation:

Suture of perforation, 56 cases, 9 deaths.

Suture of perforation and gastroenterostomy, 2 cases, no deaths.

Two gastroenterostomies, 1 without suture, 1 by plugging hole with omentum. Case without suture died.

5. Drainage:
   Cholecystectomy cases, 3.
   Gastroenterostomy, 3.
   Perforation twenty-four hours or over, 6.
   Perforation under twelve hours, 4.

Summary. For the sake of simplicity and because practically all of these ulcers were juxta pyloric, we have considered them as a single entity. A few facts may be emphasized:

1. That the duodenal ulcers, contrary to probability, give severer symptoms and a longer history. Of the patients giving a history of long standing gastric disturbance 30 per cent were gastric, 70 per cent duodenal. Of the patients giving a history of no previous trouble 65 per cent were gastric, 35 per cent duodenal.

2. The mortality from acute gastric perforation is almost double that of duodenal, namely 21 per cent to 12 per cent.

3. Duodenal ulcers give a maximum of conditions requiring further operation, 7 out of the 8 reoperated cases being duodenal. Of the 5 cases of pyloric stenosis found at reoperation, 4 were duodenal.*

TREATMENT OF SPASTIC CONSTIPATION.†

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It was Fleiner who first concentrated professional attention upon the distinction between atonic and spastic constipation. But while many authorities accept this division of chronic constipation into the two groups specified, others strongly dissent from this view on the ground that all the supposedly characteristic signs of spastic constipation are also occasionally observed in the atonic form. It is true that atonic constipation is by far the more common form, and in a considerable number of cases the two forms are associated; nevertheless the existence of a purely spastic type cannot be successfully disputed.

I shall confine this paper to a consideration of cases attributable to functional neurotic causes and the abuse of strong purgatives, disregarding for the present all the other causes of spasms of the colon, such as local inflammatory changes of the intestinal wall, adhesions, and pathological affections of remote organs.

* October 15, 1922; 4 more cases of acute perforations have been successfully operated, 2 duodenal, 2 gastric, all within the twelve-hour period.

† Read before the Annual Meeting of the American Gastro-Enterological Association at Washington, D. C., May 1 and 2, 1922.

In spastic constipation the retardation in the evacuation of the bowel is induced by a spasm (enterospasm) of a few isolated loops of the intestine. This spasm is brought about by an increased irritability of the vegetative nervous system, which may in turn be due to neuropathic conditions associated with diseases of the abdominal viscera or pelvic organs, or to either vagotonia or sympathicotonia from disturbance of the internal secretions.

The normal function of the intestine depends upon the innervation supplied by the two opposing systems of nerves, the vagus acting as the accelerator, while the splanchnics are inhibitory. In a general way we call the two systems, which are so wonderfully well balanced, the vegetative nervous system. Aside from individual variations, which may take place under normal conditions, the several organic functions may undergo far-reaching changes through excess of tonus on the part of one or the other of these sets of nerves. Every increased stimulation of the vagus results in increased activity of the muscles of the intestinal canal. Excessive stimulation, or vagotonia, induces spasm of the circular muscles of the intestine, contraction of the colon, and other phenomena.

Spasms of the colon are observed by means of palpation and roentgenographic examination. They occur most frequently at the transverse colon, hepatic and splenic flexures, sigmoid flexure, rectum, and anus. Spasm of the large intestine is important as the basis of spastic constipation, as distinguished from the atonic form. The characteristic symptoms of spastic constipation are delay in the fecal discharge, and an intestinal colic which usually precedes the defecation. In such cases there are various degrees of abdominal pain, with or without meteorism, which may affect the entire abdomen or only certain portions of the intestine. These pains are often continuous for hours, and finally terminate with the occurrence of defecation, which is often quite voluminous. It is frequently possible to palpate as a thick rope the tender contracting intestinal loops, particularly those of the descending colon and the sigmoid flexure. There is frequent desire for stool, with incomplete evacuation. Spasm may be associated with atony of the distal segments of the colon, and hypermotility or normal tonus of the proximal segments.

Spastic constipation is not to be understood as a mechanical obstruction to the passage of the feces through the intestinal canal; if it were so, hypertrophy and distention of the sections involved would result. High-grade spastic contraction is compatible with the forward movement of the intestinal contents, for it is not a permanent tonic condition. Not infrequently spastic and atonic conditions of the colon alternate or even occur at the same time, as is evidenced by the fact that the retention of feces in the ascending colon is accompanied by excessive tonus of other sections, such as spasms at the beginning of the transverse colon. When functional

constipation varies, passing from one form into another, the movements of the colon presenting different conditions at different times, we group these several manifestations together as spastic constipation.

Spastic phenomena of the colon, with or without constipation, occur more frequently in women than in men, probably because of social conditions, the nervous status in the better situated classes, and the causal relation between intestinal function and diseases of the female genital organs. This is the case especially in pronounced neuropathic individuals who are subject to organic disturbances of the gastro-intestinal tract. In the neurasthenic, functional disturbances, among them constipation, usually arise without spastic change of the intestine.

The most varied conditions of the stool coexist with spasms of the colon and of the rectum, as to form, consistency, and frequency. In spasms of the colon with prolonged haustral segmentation, the fecal matter is in the shape of irregular balls, while in proctospasm it is cylindrical or ribbon-like.

By regularly palpating the abdomen and by roentgenologic observation, strongly contracted sections of the colon may be located, especially of the sigmoid flexure and the descending colon. It is easy to distinguish between contracted and filled coils of the intestine by examining the patient repeatedly and at various times of the day. The tonus of the anal sphincter shows the presence of proctospasm, a condition which accompanies spastic contractions of the colon. The characteristic physical sign of this disease is found upon exploration of the rectum, which, instead of being filled with feces, as is common in atonic constipation, fits closely around the examining finger (proctospasm), almost like the finger of a glove. The deciding factor in the diagnosis is the roentgen-ray examination.

In the treatment of spastic constipation, the first care is to provide physical and mental relaxation for these patients, who are usually in an overstrung nervous condition. We recognize that a hypertonic state of the musculature of the stomach and intestine is a constant result in vagotonia. The intestinal canal is unduly constricted. Complete rest in bed or a fresh-air treatment is often sufficient to induce normal defecation. The principal point, however, is the prescription of a suitable diet. I recall the case of a well-known automobile manufacturer who had maltreated his intestine for years with coarse articles of diet and large doses of a variety of purgatives, with the result that he required large doses of cathartics every night. In spite of his objection and to his great astonishment, I immediately stopped all the laxatives, prescribing as a first measure a mild diet, as will be detailed later on. In the morning of the second day there was a spontaneous normal defecation, an event which had not happened in several years.

The diet in the different varieties of constipation is, on general principles, to be formulated in such a manner that a mechanical and chemical stimulation will be produced.

An active diet rich in insoluble residue is particularly indicated in chronic atonic constipation. In such cases there need be no misgivings in advising large quantities of coarse food, so long as the stomach is in normal condition. In spastic constipation the indications point to a chemically acting dietetic regimen exclusively; all kinds of mechanically irritating foods are to be absolutely forbidden. In many cases it may be necessary to occasionally administer vegetables and boiled fruit in purée form, so that our only dependence will be on the mildly laxative chemical effects of appropriate foods.

In chronic atonic constipation a coarse diet, rich in residue, to render the feces more voluminous, is prescribed to incite peristalsis. By this large and bulky diet a mechanical effect is obtained which increases the tonus of the relaxed intestinal musculature. In spastic constipation, however, the treatment is directly opposite. A diet should be selected that will make but slight demands upon the intestine. Soothing, antispasmodic foods should be administered, while the use of water and foods acting mechanically to increase intestinal motility should be excluded. No laxative should be given in the treatment of spastic constipation. Glycerin enemata and glycerin suppositories are to be strictly prohibited.

In spastic constipation raw vegetables and raw fruits containing coarse cellulose, cabbage of all kinds, mushrooms, coarse bread, Graham bread, fruit with small sharp kernels, such as gooseberries, currants and strawberries, should be avoided, as they are unquestionably likely to maintain or even increase the irritable condition of the intestinal mucosa, both mechanically and chemically. Strong spices, strong black coffee, alcohol, or carbonated cold beverages are not allowable. All beverages should be avoided which are known to have a constipating effect, such as strong tea, cocoa, claret, blackberry wine, etc. We must prescribe a soothing diet, endeavoring to render the feces pasty and soft and the intestinal mucous membrane pliant and slippery. Young vegetables, the cellulose of which is comparatively soft and tender, may be allowed, at first in the form of the finest purée and prepared with the yolk of an egg or butter. Fruit should always be stewed. Many dishes are easily made with soluble and easily digestible fats, such as cream, olive oil, almond milk, and butter. Soft fat cheese, cream cheese, and curds mixed with cream are best. Eggs are to be served soft-boiled or raw.

I prescribe a diet as follows:

Breakfast. Orange or grape fruit; porridge boiled in milk and strained, with sugar and plenty of cream and butter; weak or caffein-free coffee, or buttermilk; two ounces of cream; toast, butter, honey, jam, or fruit sauce.

Luncheon. A cup of mucoid soup; sardines in oil; tender vegetables with cream sauce; light egg dishes with vegetable purée and mashed potatoes; jam, stewed fruit (strained), or honey; cream cheese; caffein-free coffee with cream; toast and butter; lemonade sweetened with two tablespoonfuls of levulose.

Dinner. A dish of mucoid soup prepared with butter; three ounces of fowl, veal, pigeon, sweetbread, brain, tongue, tender fillet of pork or tender roast beef, or fish boiled with a free amount of butter sauce; potato purée boiled in milk and mixed with butter; macaroni prepared in butter; plenty of purée of spinach, yellow turnips, young green peas, cauliflower, or artichokes, with butter, cream or the yolk of an egg; purée of stewed fruit, cream candies, or light farinaceous dishes with fruit or cream sauce.

Mucoid soups are made from oatmeal, rice, wheat starch, potato starch, and corn starch. The grains are boiled four to six hours with water, passed through a fine sieve and again brought to the boiling point, butter or cream added, and suitably seasoned ready for use.

An immense variety of fruits must be classed among the laxatives, because of their chemical constitution. These are of particular value in cases of spastic constipation. They stimulate peristalsis partly because of their fruit acids and partly because they contain sugar, which is likely to increase the fermentative processes in the intestine. Oranges, baked apples, grapes and watermelon are valuable. Fruit and its active ingredients may be freely used as jams, jellies, fruit juices, grape juice, cider, etc. Other acids and acid foods are recommended, as citric acid, lactic acid, buttermilk, sour milk, whey, kefir (two days old), sour cream, yoghurt, vinegar, and kraut. The cases of chronic constipation reported cured by the administration of the bulgarian or acidophilus bacillus will on investigation prove to be cases of spastic constipation.

The most useful kinds of the various sugars are the easily broken-up milk-sugar and levulose. Honey induces fermentation and acts well. Easily melted fats, as butter, oil, and cream, not only have a mechanical effect, as has been mentioned, but also act chemically, stimulating peristalsis by means of the great amount of fatty acids they develop. Pure white bread is not irritating and is best. No specific directions, as a rule, need be given concerning the consumption of meat in cases of spastic constipation. Meat may be taken freely, though some authors recommend a restriction or even a prohibition of it on the ground that it induces nervous irritability.

The dietetic therapy may often be advantageously combined with certain medicaments. Large amounts of fat are capable of acting in a beneficial manner, rendering the feces soft and smooth. A. L. Benedict was the first to draw our attention to a similar effect from liquid petrolatum taken internally. These substances may therefore be employed advantageously to increase the effect of the diet. Liquid petrolatum is indicated when we desire to lubricate the

entire intestinal tract and facilitate the passage of its contents. The feces are softened and under the microscope are found to contain minute globules of the oil. Too heavy an oil should not be used, for this fails to permeate the fecal material, a desideratum as important as lubrication of the intestinal wall. The oil is not absorbed from the alimentary tract, and even in large doses has no poisonous effect. It is useful not only as a lubricant but also for healing superficial lesions of the intestinal mucous membrane. It may be given in tablespoonful doses three or more times daily.

In spastic constipation atropin or belladonna is our sovereign medicinal remedy. Atropin paralyzes the peripheral ends of the autonomic nerves and relaxes the spastic intestine. The extract of belladonna can be given three times daily in 0.008 gm. ($\frac{1}{8}$ grain) doses. In some cases atropin must be given in full doses. It may also be administered in the form of the less poisonous preparation eumydrin, the methylnitrate of atropin, in 0.001 gm. ($\frac{1}{60}$ grain) doses two or three times daily.

More recently papaverin, which is an opium alkaloid of the isochinolin group, has been recommended. According to Pal's investigations it is said to have an elective paralyzing effect upon the smooth intestinal musculature and therefore has therapeutically valuable antispasmodic properties. This preparation has been superseded by benzyl benzoate. My own experience with benzyl benzoate in doses of 1 to 2 cc (15 to 30 minims) three or more times daily justifies its use.

If the therapeutic treatment, as outlined above, should not have quite the desired effect, recourse may be had to oil enemata, as introduced by Kussmaul and Fleiner. Fleiner's oil enemata are extensively used in the treatment of chronic spastic constipation. Fleiner recommends for this class of cases one injection daily of 250 to 500 cc ($\frac{1}{2}$ to 1 pint) of the purest olive oil. The oil is to be retained in the bowel for a considerable time; it is best to retain it over night if possible. Should discomfort during the night (meteorism, pressure) result, as may occasionally happen, the time of administration should be changed, the enema being given at six or seven o'clock in the morning while the patient is in bed; the oil is then to be retained for three or four hours, thus producing the same laxative effect as if it had been administered at night.

These injections should be continued for several months, at first daily, later every other day, and subsequently twice a week. The results are so good that in many cases of spastic constipation actual recovery is brought about without any other treatment. The oil, by partially breaking up into fatty acids, stimulates peristalsis; and it has a soothing effect on the tense muscular tissue. Besides it lubricates the gut, softens the fecal agglomerations, and forms a protective layer upon any inflamed portion ot the mucous membrane.

As a rule no discomfort is caused by the "oil cure," and the

patients are at the time hardly aware of the fact that the oil is being introduced. It has not been ascertained definitely whether the oil passes beyond the ileocecal valve in all cases, but some patients experience the taste of oil after receiving a number of enemata. The only inconvenience caused by the oil enemata is the impossibility of avoiding the soiling of the bed and the bedclothes. The patient must remain in bed for at least an hour after the injection, without indulging in much conversation, coughing, or laughter. Should there be no spontaneous action of the bowels in the morning, a small lukewarm sodium-chloride water enema should be given.

Massage is contraindicated in spastic constipation, and all energetic manipulation aggravates the condition. Nor is the use of mechanical vibratory massage of any value in this form of constipation. All abrupt changes of temperature and all forms of mechanical irritation are to be guarded against. Warm applications made to the abdomen frequently overcome the spasms. A Priessnitz abdominal bandage may be applied over night, and a hot water bottle or electric pad placed upon the abdomen several times during the day.

THE DIAGNOSIS AND TREATMENT OF INTESTINAL OBSTRUCTION.[1]

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Until an antidote is discovered for the toxemia of acute intestinal obstruction, this lesion will remain the most fatal of all acute abdominal crises. The mortality has not been greatly diminished by aseptic surgery and whatever improvement may be noticed in the later statistics can be credited to the performance of an operation in an earlier stage of the condition, rather than to improvement in technical procedure. Recognition of the condition in this earlier stage therefore, becomes the most important factor today in the cure of the patients by prompt operation.

Acute intestinal obstruction is the sudden arrest of the passage of the contents down the intestinal canal. Any one of many causes may be responsible for its development. The position and character of the obstructing force are important factors in determining the severity of the symptoms and the time of the fatal result. It is generally agreed that the higher the obstruction, the more severe the symptoms and the more rapidly fatal the disease. Strangulation, or other interference with the circulation

[1] Read at the meeting of the American Gastro-Enterological Association in Washington, May 2, 1922.

increases the severity of the condition, at the same time adding to the probability of the fatal result. The more serious symptoms appear to be the result of the absorption of toxins from the obstructed bowel. The toxemia and the efforts of the gastro-intestinal organs to overcome the obstruction produce a series of symptoms which are grouped together under the term ileus.

Ileus, therefore, may be the result of many conditions all of which obstruct the flow of the intestinal contents. Reflex and toxic paralyses, spastic contracture, as well as mechanical obstructions, either from within or without the bowel, may be the underlying cause. The mechanical form always requires operation, the paralytic rarely; and the spastic type, while occasionally operated on, probably represents those cases in which spontaneous relief occurs.

The greater intensity of the toxemia in the presence of vascular disturbance is in part due to the resultant change in the intestinal wall. The peculiarities of the mesenteric circulation, especially the results of occlusion or patency of the parallel artery of the small intestine, play a large part in determining the effect of the obstruction.[2]

It is difficult to imagine an obstruction of long duration from any cause in which the intrinsic blood supply has not been affected by the distension and distortion of the bowel wall. Such circulatory change may account for the sudden onset of acute symptoms in cases of long-standing partial obstruction.

Whenever the underlying cause of an obstruction is of such a character that it can be recognized and removed early in the disease, the severity of the toxic symptoms is diminished, or their development is prevented. In strangulated hernia, where a painful external swelling calls direct attention to the obstruction, operation is performed in most cases before toxemia develops. The irreducible external swelling focusses attention on the obstruction and brings the patient to operation without delay. Although certain other conditions may be responsible for the protrusion, these are quickly excluded, or recognized as lesions which require operation for their cure.

Similar reasoning should bring the internal obstructions to early operation. In spite of the fact that there are no signs so distinct as the external hernial swelling, the symptoms of intestinal obstruction are well defined and with proper interpretation it is often possible to make a diagnosis before the onset of grave toxemia.

Symptoms. It is convenient to divide the symptomatology and course of acute intestinal obstruction into three stages:[3]

(1) The stage of onset, when the symptoms are due to the arrest

[2] Murphy, J. B.: Jour. Am. Med. Assn., 1896, **26**, 15.

[3] These stages do not represent any definite period of time. In twenty-four hours a patient may pass through all three and die of toxemia.

of the intestinal current; (2) the stage of compensation, when the gastro-intestinal organs attempt to overcome the obstruction or its results; (3) the stage of sequelæ or complications, when the obstruction has caused secondary destructive changes in the bowel, or in the body as an entirety. The higher and more complete the obstruction the less clearly defined will be the symptoms of the various stages. Vascular injury always intensifies the course of the disease. Gangrene of the bowel may either complicate the compensatory effort, or be present with the toxemia.

The characteristic symptoms of onset are pain, constipation or diarrhea, and vomiting. The pain is paroxysmal, with free intervals, or it may be continuous between the exacerbations. This paroxysmal pain, usually described as cramps, is the most constant initial symptom and becomes increasingly severe during the first hour. The pain of obstruction is not relieved by defecation or by vomiting. Opium brings only temporary ease. Constipation may be absolute, or there may be an initial bowel movement preceding the onset of pain. The constipation resists well given enemas, or an effectual enema does not give relief from the pain. Tenesmus, or diarrhea and pain with blood and mucus in the stools occurs in certain cases of strangulation, with intussusception, and with intestinal tumors.

Vomiting may be the initial symptom, followed by pain and constipation, but the usual sequence is pain, vomiting and constipation. The vomited material may be gastric or duodenal contents. As a rule, however, the material is first gastric, then bilious, and finally intestinal. At the onset it is gastric occurring without regard to the ingestion of food. Lavage does not relieve the symptoms. The initial vomiting is reflex, and may be replaced by hiccough.

The blood-pressure practically always falls as the symptoms develop; occasionally there is a rise in the pressure during this initial stage. A falling pressure indicates the onset of intoxication.

The symptoms of the second stage are local and general. The pain becomes more intense, unless gangrene develops, in which event it may be diminished. The vomitus of the second stage consists of material flowing back into the stomach from the obstructed intestine. The quantity vomited may be extremely large. There is a great increase in the amount of fluid secreted by the obstructed intestine. The fluid is thin, acrid, disagreeable in taste and odor, and is irritating to the mouth, lips and chin. The color seems to darken with the duration of the obstruction, passing from yellow through green to dark brown.

Visible peristalsis or visible and palpable, stiffened intestinal coils are the most characteristic symptoms of the second stage. The stiffened coil is a distended area in which the contractions have reached the tetanic stage, and in which there has occurred

an infiltration of the wall with an accumulation of fluid and gases in the interior of the bowel. Visible peristalsis is due to an extraordinary activity of the bowel produced at this time. The movements are vigorous and associated with the presence of the visible stiffened coil. When much small intestine is involved in the process, the spastic distended coils may show as a series of parallel ridges, the ladder pattern. The contractures are accompanied by pain unless the toxemia has become grave.

The early distention is regional and usually asymmetric. Later there will be general distention. Tympanites accompanies distention. The lower the obstruction the greater the distention and tympanites. Local tenderness may indicate the soreness of spastic muscle, or may be from a local peritonitis at the point of obstruction. The blood-pressure falls during the second stage.

In the third stage the symptoms are those of toxemia, gangrene, peritonitis and alteration of the function of the liver and kidneys.

The toxin of intestinal obstruction is a virulent poison, although there appear to be individual variations in resistance to it.

The rate of the pulse and respiration is increased, the blood-pressure falls; there is great prostration and cyanosis with or without clammy skin. The mental condition varies from noisy delirium to unconsciousness. Often there is a subjective sense of well being, contrasting greatly with such objective signs as regurgitation of stercoraceous material, and distended abdomen in which violent peristaltic action is visible.

The development of gangrene is accompanied by collapse, and often sudden and severe increase of pain, although later the pain is diminished. As a result of leakage, peritonitis ensues and with its spread comes movable dulness in the flanks and obliteration of liver dulness.

Peritonitis is the result of invasion by the intestinal bacteria either through gross rupture of gangrenous bowel, or by penetration of the bacteria through an area of intestine whose wall has been altered by distention or constriction. The absorbed toxin probably reaches the circulation through the lymphatics. The liver seems to be involved in the defense of the body, but the changes produced in this way are not yet explained. The kidneys probably make an attempt to excrete the toxin from the blood, and in this way certain changes in their function are brought about. The intestine itself is involved in this process of excretion, which therefore brings about a vicious circle.

Laboratory Studies. Laboratory examinations are not of great value in diagnosis, although the following estimations may prove helpful:

The Blood Count. Usually there is a marked leukocytosis. In a series of 62 cases the average was 16,000; in but 2 was it below

5000, and in 7 others below 10,000. The highest was 46,000 in a case of volvulus of the sigmoid.[4]

The Non-protein Nitrogen in the Blood. In obstruction the quantity of this nitrogen in the blood is increased. Certain variations have been noted by experimenters which indicate that a series of observations made every four or six hours will give better information than a single estimation. If the successive examinations show an increase operation is indicated, while in the presence of a falling or stationary quantity delay seems justifiable.[5]

Unfortunately many of the lesions in which a differentiation from obstruction is difficult give similar changes in the blood nitrogen, or make a diagnosis so urgently necessary that delay for repeated examinations cannot be afforded.[6]

The Urine. Albumin and casts are frequently present from the onset of symptoms and are found in all cases of severe toxemia. The casts disappear from the urine after the obstruction has been relieved.[7] Indol and skatol derivatives are present in the urine in obstruction, but they are also present in so many other conditions that their estimation is of no value in diagnosis.

The foregoing are the general symptoms of intestinal obstruction. No attempt has been made to give signs which will separate the variations in the condition which depend on differences in etiological factors. Such signs exist and usually may be interpreted with ease, but no time should be lost in searching for such differential points. The diagnosis of acute intestinal obstruction as an entity is sufficient indication for operation.

Differential Diagnosis. The differential diagnosis between intestinal obstruction and other lesions having similar symptoms becomes most important when we are called on to separate the conditions which require operation for their cure from those in which operation is not necessary, or in which it may be even harmful. In the former group of cases it may be impossible to make an accurate diagnosis beyond the recognition of the crisis, which demands immediate intervention. The exact nature of the trouble in such cases must be decided upon after the abdomen is open. Delay for academic accuracy of diagnosis wastes the opportunity for curing the patient before the development of complications which make the use of disagreeable expedients necessary.

Abdominal Symptoms of Thoracic Disease. The onset of pneumonia, of diaphragmatic pleurisy, of pulmonary infarction, of pericarditis, as well as the acute exacerbations of cardiovascular disease may be ushered in by marked abdominal symptoms, which

[4] McGlannan, A.: Jour. Am. Med. Assn., 1913, **60**, 733.

[5] Vaughan, J. W., and Morse, P. F.: Arch. Surg., 1921, **3**, 403. Stone, H. B.: Surg., Gynec. and Obst., 1921, **32**, 415.

[6] Bacon, D. K., Anslow, R. E., and Eppler, H. H.: Arch. Surg., 1921, **3**, 641. Louria, H. W.: Arch. Int. Med., 1921, **27**, 620.

[7] McGlannan, A.: Loc. cit.

may closely simulate those of the first stage of intestinal obstruction, or be accompanied by distention and other signs of the toxic stage.[8] Throat infections in children may simulate abdominal disease.[9]

Rontgen-ray examination of the chest will often show the lung lesion and will aid in recognizing the cardiovascular ones when physical signs are indistinct. Levine[10] notes in the confusing cardiac lesions a small thready pulse with slight increase in rate and a regular rhythm, but quite distant heart sounds. The development of a slow pulse and fainting attacks points directly to a cardiac condition. If the patient is over forty with a history of dyspnea and there are any physical signs of cardiac enlargement, the probability of a thoracic rather than an abdominal cause for the symptoms becomes greater. When the apparatus is available, the electrocardiogram may add to the certainty of the heart lesion.

If the area of pain and tenderness be carefully mapped out, and the patient then be directed to hold his breath, the pain and tenderness will be absent as long as the diaphragm remains quiet.[11] In the absence of other signs of thoracic disease, abdominal pain associated with movements of the alæ nasi during respiration indicates a thoracic and not an abdominal lesion. The anxiety in the case of the thoracic lesion is lethargic and resigned, not terror stricken and active as in the abdominal conditions.[12] If the possibility of thoracic disease as the cause of the symptoms is kept in mind, a mistake in their interpretation is unusual. During an epidemic such mistakes are rare.[13]

The crises of tabes are often associated with distention of the abdomen. The characteristic changes in the pupil and in the other reflexes make the recognition of the tabes definite.

The visceral crises of angioneurotic edema may simulate an acute obstruction. The presence of blood in the stools may lead to the suspicion of intussusception or tumor. The history of previous attacks, or the association with symptoms of hives, of purpura, or other superficial manifestations of the condition will make the diagnosis.[14] Blood in the urine is suggestive of the angioneurotic lesion rather than obstruction. The non-protein nitrogen of the blood is not increased in tabes or in angioneurotic edema.

Acute Dilatation of the Stomach. In this condition the pain is continuous and referred to the chest wall. The distention is epigastric. There is no vomiting, but rather a regurgitation of discolored fluid. Lavage gives immediate relief from the symptoms.

[8] Brooks, Harlow: Med. Record, 1921, **100**, 1103.
[9] Brenneman, J.: Surg., Gynec. and Obst., 1922, **34**, 344.
[10] New York State Jour. Med., 1921, **21**, 382.
[11] Asserson and Rathbun: U. S. N. N. Med. Bull., No. 1, p. 29.
[12] Smith, R. E.: Lancet, 1919, **1**, 421.
[13] McGlannan, A.: Surg., Gynec. and Obst., 1920, **30**, 462.
[14] Dwyer, H. L.: Jour. Am. Med. Assn., 1922, **78**, 1187.

Adrenal Disease. Destruction of the adrenals by disease and experimental removal of these bodies both give rise to certain symptoms resembling those of the toxic stage of obstruction. The action of the toxin of obstruction is almost identical with that of acetylcholin, which substance acts as a physiological antagonist to the suprarenal secretion. The development of analogous toxic symptoms after the destruction of the adrenal bodies points to some antagonism between the substances and indicates the value of epinephrin in the treatment of patients suffering from obstruction with toxemia. The diagnosis between the conditions can only be made by identifying the preëxisting adrenal disease.

Spastic Ileus. Spasmodic contracture of a segment of the bowel occurs in lead poisoning, in certain tabetic crises and as the result of a number of reflex irritations. The obstruction may become so complete as to lead to toxemia and death. As a rule the symptoms are intermittent, but they may be continuous and rapidly progressive. The condition is often observed after operations in or near the peritoneal cavity, for example, after lumbar nephrectomy. Apparently a spastic obstruction may be the beginning of an intussusception, the contracted segment being thrust into the lower loop.[15] The differentiation between spasmodic and mechanical obstruction cannot be made from clinical investigations and therefore in all cases where the symptoms are urgent, operation should be performed and the diagnosis made after the abdomen has been opened. The spasm usually relaxes spontaneously, or as the coils are handled. This fact may account for some of the cases diagnosed as obstruction in which laparotomy has failed to reveal any lesion.

Mesenteric Vascular Occlusion. The occlusion may be arterial or venous, embolic or thrombotic. A combination of injury and infection is the usual cause. The symptoms are very like those of acute obstruction. At the onset the vascular lesion is usually associated with greater shock and there is apt to be a passage of a considerable quantity of blood and fecal material. The distention is general and is seldom as great as in obstruction. Some cases diagnosed mesenteric thrombosis or embolism have recovered without operation, but as a rule it is better to open the abdomen and deal with the condition surgically.

Acute Pancreatitis. The history of long standing gall-bladder disease in an obese individual, who has an acute abdominal crisis, especially if the attack is associated with cyanosis and great collapse, will lead to the suspicion of pancreatitis, but the diagnosis is never certain until the fat necrosis is found after the abdomen has been opened. Therefore no time should be lost in attempting a distinction between this lesion and an acute obstruction. If, as

[15] Freeman, L.: Ann. Surg., 1918, **68**, 196.

Ellis[16] indicates there is a close relation between the toxin of acute obstruction and that of pancreatitis, the differentiation between the lesions approaches the impossible.

Ruptured Abdominal Viscus. After the original collapse, the symptoms of ruptured viscus are those of spreading peritonitis rather than of obstruction. The continuous pain and the board-like rigidity of the abdomen are the best signs for differentiation. Similar symptoms are associated with rupture of an ectopic pregnancy. In this lesion the menstrual history usually helps. The signs are more marked in the lower abdomen, and a pelvic examination may make the diagnosis certain. Bluish discoloration of the umbilicus when present indicates ectopic pregnancy.[17]

Torsion of a pedicled tumor may give symptoms resembling those of obstruction. In the early stage the presence of the tumor will indicate the character of the lesion. In the late stage, a reflex paralytic ileus may complicate the picture. While this condition makes accurate diagnosis doubtful, it gives a clear indication for the necessary treatment, namely operation.

The onset of appendicitis, of cholecystitis and certain types of kidney colic may give symptoms very like those of acute obstruction. With the inflammatory lesions there is usually fever, and there is less shock than in obstruction. The character of the pain is continuous and there is local tenderness and much spasm from the onset of the attack. Appendicitis in older persons is apt to begin with obstructive symptoms.[18]

Kidney colic is associated with blood in the urine, either grossly or microscopically. There are usually other symptoms referred to the urinary tract, as for example, vesical tenesmus.

Peritonitis. The differentiation between peritonitis and intestinal obstruction is usually difficult and often impossible. Laboratory examinations do not help and the clinical signs are likely to be confusing. A local peritonitis by infiltration of the bowel wall can set up an obstruction. The fulminating type of peritonitis causes a paralytic distention of the intestine with stoppage of its contents. A tightly strangulated bowel will allow the passage of infectious material through its damaged wall and thus set up a local peritonitis.

At the onset the continuous pain of peritonitis contrasts with the paroxysms of obstruction. Muscle spasm and rigidity of the abdominal wall are prominent symptoms in peritonitis and are absent in obstruction. Fever is more likely to be present in peritonitis, and peristalsis is lessened. The development of distention in a quiet abdomen indicates peritonitis, and makes a contrast to

[16] Ann. Surg., 1922, **75**, 429.

[17] Cullen, T. S.: Contributions to Medical and Biological Research, dedicated to Sir William Osler, in honor of his seventieth birthday, 1919, **1**, 420.

[18] Bottomley: Ochsner's Surgical Diagnosis and Treatment, 1921, **3**, 55.

the noisy abdomen of obstruction with its visible peristalsis and palpable distended coils. The distinction between peritonitis and obstruction is most important in postoperative cases. Occasionally the nature of the primary operation gives a clue as to the more probable complication. It is possible that a rapidly increasing quantity of non-protein nitrogen in the blood may be characteristic of obstruction rather than of peritonitis.

TREATMENT. With these facts in mind, therefore, how shall we proceed when called on to treat a patient who is suddenly seized with paroxysmal abdominal pain, nausea or vomiting, and disturbance of the bowel movements?

The onset of an acute thoracic lesion, or one of the cardiac upsets should be considered and decided. Unless the lesion above the diaphragm is definitely recognized, the attention should be focussed on the abdomen. Lead colic, angioneurotic edema and tabes are recognized by their extra abdominal symptoms.

The physical examination will determine the presence or absence of masses, tender points, local distention, etc. A ballooned rectum suggests a low obstruction. An empty rectum, or one containing only a little feces, is found with obstruction of the small intestine. The presence of a large quantity of feces, especially if the material be hard, indicates a coprostasis rather than an obstruction. Severe symptoms however are rare in cases of fecal impaction. The obstructed loop may be felt through the rectum.

An enema should be given by a competent person, and the stomach emptied by lavage. If an effectual enema does not bring relief from the pain, the suspicion of a mechanical obstruction becomes very strong. Similiarly gastric lavage which does not bring relief points to an obstruction. If the pain continues, both enema and lavage should be repeated after an hour. If the second enema is retained, or escapes unaltered and with slight force, the presence of an obstruction becomes certain. If the second lavage brings away duodenal contents, the diagnosis is made even more certain. Under such circumstances operation is the proper treatment.

As a rule these tests are sufficient to lead to a diagnosis. In 18 cases of postoperative intestinal obstruction an operation was performed after the diagnosis had been made on these symptoms. In every case a mechanical obstruction was found and relieved and all these patients recovered.

Should the effect of the enema and lavage fail to be convincing, corroborative evidence of obstruction may be furnished by a rise in the quantity of the non-protein nitrogen in the blood. In the doubtful cases repeated blood studies at four-hour intervals are valuable. During this period of doubt the patient should be in the hospital, prepared for operation. The time may be employed in repeating the enema and lavage.

Cathartics are so dangerous that it has become a rule to prohibit their use in the presence of symptoms of obstruction.

Opium is banned, because it may mask symptoms.

In managing the patient in whom an obstruction is suspected, the judicious use of opium or a cathartic may be employed during this period of doubt. After the stomach has been emptied by lavage 2 or 3 ounces of castor oil is poured in through the tube. At the same time $\frac{1}{32}$ of a grain of eserin salicylate, or a dose of pituitrin is given hypodermically. In the presence of mechanical obstruction this treatment intensifies the primary symptoms and hastens the development of the secondary ones to such a degree that the diagnosis becomes certain, and operation imperative. On the other hand, relief of the symptoms ends the uncertainty.

SOME UNAPPRECIATED FINDINGS IN THE LUNGS OF NORMAL CHILDREN.

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and

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The practical object of diagnosis is to distinguish between healthy and morbid physical conditions. Diagnostic ability depends as much or more upon an accurate recognition of the non-significant normal variations in health as upon an appreciation of the manifestations of disease. The latter can evolve only as a corollary of the former.

To Auenbrugger and to Laennec we owe our earliest knowledge of the "physical means of exploration" of the chest. To Wintrich, Skoda, Gerhardt, Flint, Sahli and to a host of others, we are indebted for the elaboration of our understanding of thoracic diagnosis. Yet, even at this late day, all the physiological variations from the normal are not recognized, and, as a consequence, an unwarranted diagnosis of disease oftentimes results.

In a clinical and roentgenographic study of normal children, it was found that variations from the usually accepted findings in health were often present, and it is our purpose to emphasize the need of evaluating such findings as physiological and not as evidence of disease.

The clinical data dealt with in this report were obtained by careful examination of more than 200 apparently healthy children

between the ages of six and ten years.[1] All children who showed signs of disease were excluded from the series. Individuals from various strata of society were studied: foreign and native born, residents of urban and of rural communities, school children and children residing in institutions, children exposed to tuberculosis and some without a history of such exposure, children with and without a history of previous infectious diseases, all symptom-free, and of an approximately normal height and weight for their ages. A history of each individual was recorded and in making the examination of the chest, care was always observed to have the child relaxed and to see that no cramped or unnatural posture was assumed, for, as is well known, faulty position may lead to findings that cause confusion in interpretation. A roentgen-ray examination of the chest was then made. In addition, a tuberculin test was made on every child. The clinical data were then assembled and after the roentgenologist had interpreted his plate independently, the clinical and roentgenographic findings were correlated.

Our observations disclosed in many the signs generally described as usual in healthy children. In addition, however, we have found on percussion, on auscultation and by examination with the roentgen ray, some changes not generally recognized as within the range of normal before the age of ten years and often incorrectly estimated as indices of pathological change. Only these findings will be considered here.

It is generally stated that the percussion note elicited over the lungs of normal children within the age limits under consideration is fuller, more tympanitic, of higher pitch and more resilient than that noted over those of adults, and that frequently the tympanitic quality is quite outspoken, especially over the lower lobe of the left lung. Although in general our observations confirmed this view, we have been impressed by the fact that in an appreciable number of such children, the note obtained on percussion over the lungs is indistinguishable in quality from that elicited over the lungs of normal adults and that the usual resilience of the note is lacking. These findings in many instances have an analogue in shadows noted in the roentgen-ray films, shadows indicative of increased density along the bronchial tree, similar to those seen in the plates of normal adults. This correlation of the findings on physical examination and on roentgen-ray study is more constantly

[1] The observations reported were made during a period of several years. They have been established in the course of a study undertaken at the suggestion of and under a financial grant from the National Tuberculosis Association. It is part of a report of a Research Committee consisting of Drs. H. R. M. Landis and H. K. Pancoast, of Philadelphia; K. B. Blackfan and K. Dunham, of Cincinnati; and C. R. Austrian and F. H. Baetjer, of Baltimore. The complete report of this committee is to appear in the Transactions of the National Tuberculosis Association for 1922.

possible in studies of the upper half of the chest. When minor changes, similar to those discovered by roentgen-ray examination of the upper lobes, occur in the bases, they usually escape detection by physical examination. In those instances, in which no shadow is found to explain the deviation of the note from the generally accepted one, it is our belief that the lack of resilient quality may be due to a decreased elasticity of the chest wall.

The so-called tympanitic quality of the percussion note over the left base may be increased, decreased or be entirely lacking, depending upon the degree of distention of the stomach or colon, the curvature of the spine, and may likewise vary with the position of the diaphragm or with the posture of the child during the examination. The note over the upper thorax is often the same on the two sides.

A barely detectible diminution of resonance over the spical regions is of no significance unless associated with a modification of the breath sounds in those areas or with other abnormal auscultatory findings.

It is generally accepted that normally in childhood the breath sounds have a harsh, sharp character, with expiration longer and better heard than in the normal adult. This so-called puerile breathing is physiological and though it may seem trite, let it be emphasized that this exaggerated vesiculo-bronchial respiratory murmur, especially well heard in the areas overlying the great bronchi (*i. e.* anteriorly at the level of the first interspace and the second rib just lateral from the sternal margins, and posteriorly, particularly on the right side, at the level of the second to the fourth spine) is often incorrectly interpreted as evidence of pulmonary disease. An auscultatory finding that has not been pointed out, or at least, has not been emphasized, has come forcibly to our attention in carrying out this study. Just as the full, deep note of higher pitch characteristically elicited by percussion of the child's chest is often replaced in health by a note more like that produced when one percusses the normal chest of an adult, so, on auscultation of a child's normal lungs, the exaggerated or puerile breath sounds may be lacking, and instead the so-called vesicular respiratory murmur characteristically present in adult life is heard. This finding, regarded by us as a physiological variation, has been noted as early as the age of four years and may perhaps occur in younger children. It is more readily appreciated and more often found than the variation in the percussion note just described. In more than 50 per cent of the children in which this type of breathing was heard, examination with the roentgen ray gave findings like those obtained by a study of normal adult chests. In fact, the agreement of clinician and roentgenologist was so constant, that on the basis of these variations they are often able to designate the chest of normal children as of "puerile" or of "adult" type. The essential

fact to be stressed is that so-called vesicular respiration is heard with great frequency in normal children, and is to be regarded as a variation of normal and not necessarily as an indication of disease.

These variations and those of the percussion note are more generally found in children with a history of infections of the respiratory tract. No satisfactory explanation for this finding is offered. It may be due in part to altered resilience of the chest wall, a suggestion supported by the fact that in some instances in which it was noted, diminished elasticity of the thoracic wall was apparent on percussion. It may depend upon variations of elasticity of the parenchyma of the lung. It may be due to a relative narrowing of the lumen of the bronchial tree. It is hardly to be considered evidence of increased density of respiratory tissue, for, theoretically, at least, that should lead to a modification toward bronchial breathing.

The whispered voice sounds normally are transmitted loudly and often syllabation is heard over the region of the major bronchi. Auscultation of these sounds over the upper thoracic spine of the children has led to the conclusion that d'Espine's sign as indicative of enlarged tracheo-bronchial lymph nodes is, to say the least, of doubtful value. In 23 of the children, this sign was elicited without other signs of a mediastinal mass and without any corroborative evidence on roentgen-ray examination. In 3 children the sign could not be elicited, although from the roentgen-ray plate it might have been inferred that it should be. The presence of this sign, together with a slight diminution of resonance in the interscapular region is all too frequently made the premises for a diagnosis of tuberculosis of the tracheo-bronchial lymph nodes.

Further roentgen-ray examination of normal children within the age limits mentioned has reëmphasized the role that antecedent healed infections may play in the production of areas of increased density within the respiratory tract (bronchial tree, parenchyma of the lungs, etc.). Not only may recognized or remembered infections of the bronchi and lungs be responsible for alteration in these tissues, but other diseases not ordinarily considered of significance in this regard may be the cause of such changes. Our observations indicate that after measles, pertussis or tonsillar infections, areas of increased density radiating from the hilum into the bases especially, often occur. Such lesions generally are not discoverable on physical examination and would be unsuspected but for the use of the roentgen ray. This finding emphasizes the need of a careful history as well as examination in all individuals, before proceeding finally to interpret the findings of the roentgenologist. By way of digression, it may be interesting to point out the fact that though measles and pertussis have been known to produce lesions in the upper air passages, involvement of the lower

tract has been considered a complication and was thought to occur only when evidences of bronchitis or of broncho-pneumonia were discovered. Our observations indicate that there may be a mild inflammatory process throughout the respiratory passages in a large percentage of the so-called uncomplicated cases of these diseases. This suggestion warrants further study in relation not only to the infections under consideration but also other infectious diseases. That such shadows, mediastinal and basal, noted in children who give a history of uncomplicated measles and pertussis are evidences of healed processes is evidenced by our experience that similar shadows of like origin have remained unchanged and without the development of clinical symptoms in a series of children observed over a period of from three to five years. Such changes must be properly evaluated as indices, not of present disease, but of lesions past and healed, not as warrants for the diagnosis of present illness and the institution of treatment, but as scars of infections met and overcome.

Conclusions. 1. The data obtained on percussion and auscultation of the lungs of normal children show wide variations from a fixed standard. These variations are usual and are considered to be within normal limits.

2. Failure properly to evaluate these deviations from a fixed standard will often lead to the unwarranted diagnosis of disease and to the institution of even less justifiable treatment.

3. D'Espine's sign as indicative of enlarged tracheo-bronchial lymph nodes is of little value.

4. Inasmuch as shadows noted in roentgenograms of the chest of healthy children are dependent often upon alterations that persist as the residua of past infections of the respiratory tract, it is obvious that a careful anamnesis with special reference to all infections is necessary if diagnostic errors are to be avoided. Even a history carefully taken is often unreliable, as minimal infections are soon forgotten by many and among the unintelligent classes even more significant indispositions are not readily recalled.

5. With a proper appreciation of the widest variations that the normal may present from the ideal, the informed clinician is better able correctly to understand the findings of the roentgenologist, and each, coöperating with the other, is less liable to error.

6. Recognition of and familiarity with the foregoing data is of cardinal and practical importance to every patient, potential and established. Without a proper appreciation of the facts set forth, no intelligent differentiation between a normal and an abnormal respiratory tract can be made.

PLEURO-PULMONARY REFLEX: ITS ETIOLOGY, PREVENTION AND TREATMENT.

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The general belief that exploratory thoracentesis is a perfectly safe procedure has undoubtedly influenced many of us to resort to this diagnostic measure with a frequency not entirely warranted by the positive results obtained. Indeed, it is a matter of common knowledge that even in the most reputable hospitals a great many exploratory punctures yield negative results and might have been omitted had the clinical data been studied with more care and thoroughness. However, it is not the promiscuous use of this procedure insofar as it betrays wrong diagnoses that prompts this discussion; it is the fact that accidents and even fatal issues may follow ordinary thoracentesis, especially in dry taps, that prompts the serious consideration of this subject.

First and foremost among these distressing occurrences is pleuro-pulmonary reflex, a symptom-complex, characterized by cardio-respiratory failure, tonic and clonic contraction of the body musculature and loss of consciousness which may appear with amazing and dramatic suddenness in the course of pleural puncture and may even cause death.

To Rogers[1] we are indebted for the first description in 1864 of a case of pleural reflex in a girl who, in the course of exploratory pleural puncture was seized with an "eclamptic fit." Raynaud[2] in 1875 recorded 2 similar cases and expressed the belief that such occurrences are more common than the literature on the subject would indicate.

Soon after numerous cases were noted, so that in 1905, Roch[3] was able to collect 39 such cases, and five years later Cordier brought up the total to 84. Dayton,[4] in 1911, in an excellent monograph collected 23 cases in which pleural reflex occurred as a result of ordinary thoracentesis, 15 of which ended fatally. Zesas,[5] in 1914, summarized 54 cases of which 45 exhibited tonic and clonic contractions in addition to cardio-respiratory disturbances. 7 of the 21 fatal issues of this series followed ordinary exploratory puncture.

With the increase in the number of patients treated with artificial pneumothorax there have appeared in recent years numerous reports of the occurrence of this distressing symptom-complex. so that in 1915 Sachs[6] was able to collect 22 such cases among 1122

patients so treated by twenty-four American authors. Forlanini[7] has met with 12 such instances in his 134 cases, and Saugman[8] in seven and a half years encountered 22 such accidents all together; 6 of these were mild and 2 ended fatally. Similar cases were reported by Brauns,[9] Beggs,[10] Lyon,[11] Giese and Conwey,[12] Stivelman,[13] Castle,[14] Unverricht[15] and others.

ETIOLOGY. In estimating the dangers of thoracentesis it is important to take into consideration those instances of severe and fatal accidents which might have occurred without any interference. It has been pointed out by Weill,[16] Brouardel[17] and Lichtenstern[18] that sudden death in pleurisy with effusion is not uncommon. Brouardel records the case of a man who was being prepared for an exploratory thoracentesis, but died as the physician was entering the house. Had he lived a few minutes longer the pleural puncture would have been held accountable for the fatal issue. It must be pointed out, however, that the postmortem examination in such cases reveal pathological processes which are in themselves incompatible with life, namely, extensive thrombosis of the heart or pulmonary arteries, advanced myocardial changes, extreme cardiac displacement and torsion of the larger vessels due to copious effusion and edema of the sound lung.

It is different in the case of pleuro-pulmonary reflex. Here no such pathological lesions are discoverable. Moreover, inasmuch as this reflex most frequently follows thoracentesis yielding negative results, *i. e.*, in the absence of pleural effusion the distressing symptoms attended therewith cannot be explained on the basis of pathological processes due to or resulting from extensive effusions. It is not surprising therefore, that numerous theories have been promulgated in hope of throwing some light on the etiological factors concerned in the production of this distressing symptom complex.

Lemoine[19] is of the opinion that these accidents in the course of pleural puncture are mere coincidences. Brauer[20] still adheres to the idea that gas embolism is the cause of symptoms attributed to pleuro-pulmonary reflex. These views however, seem erroneous, inasmuch as they fail to explain the fact that these symptoms have a tendency to repeat themselves with each succeeding pleural puncture.

Absorption of toxic material has been considered an etiological factor, but as a matter of fact these distressing symptoms frequently occur at the very instant the needle is inserted before absorption of anything is possible.

Status lymphaticus has been suspected as a causative factor,[21] but autopsy findings in children who have died suddenly in the course of thoracentesis fail to lend any support to this view.

Rapid removal of large quantities of pleural exudate may give rise to severe cardio-respiratory embarrassment, but since pleural

reflex is particularly liable to follow dry taps, it cannot be explained on the basis of sudden displacement of the mediastinal organs consequent to aspiration.

Those who have encountered the accident in the course of induced pneumothorax have attempted to explain it along different lines. The inflation of the pleural cavity with gas which is below the body temperature has been expressed as a contributory cause,[22] yet this accident occurs most frequently in cases where inflation is not attempted and all methods fail to reveal the presence of air in the pleural cavity. Others maintain that imperfect anesthetization of the needle tract predisposes to pleural reflex. Against this is the fact that this reflex occurs as often after complete anesthetization of the needle tract as when no anesthetic is used at all.

The first intimation of the reflex origin of this symptom-complex was made by Leudet[23] as early as 1876. He recorded the interesting observation that epileptic convulsions, cardiac syncope and coma may follow the introduction of a sound into the pleural cavity of a patient operated upon for the relief of empyema.

von Saar[24] has obtained movements of the upper limb by irritating the parietal pleura, and Davies[25] is of the opinion that syncopal attacks are produced reflexly, as a result of irritation of the pleuro-pulmonary tissue.

Orlowsky and Fofanow[26] express a similar opinion and Langendorf and Zender[27] have succeeded in producing symptoms ordinarily ascribed to pleural reflex by irritating the peripheral ending of the vagus nerve.

Cordier[28] records an interesting experiment. After cutting the right vagus nerve of a rabbit, he injected 4 cc of tincture of iodine into its right pleural cavity. No reaction whatever followed. He then injected 2 cc of tincture of iodine into the left pleural cavity and convulsions occurred almost immediately. Autopsy findings failed to disclose any lesion in the heart, lungs or brain.

Brodie and Russell[29] in extensive experimental investigations have found that the pulmonary nerve fibers at the root of the lung in the bronchial tubes and alveoli would respond to electrical stimulation with a more powerful cardio-inhibitory action than any other of the branches of the vagus. But since they found no effect on the blood-pressure from stimulations of the healthy pleura, they concluded that the irritation of the inflamed pleura will not give rise to reflex phenomena.

In connection with the data just referred to, it occurred to me that the experience gained from pleural punctures in the course of therapeutic pneumothorax might shed some light not only on the symptomatology and frequency but possibly also on the etiology of pleuro-pulmonary reflex. I have therefore analyzed the data accumulated in the last five years during which period there have been performed at our sanatorium 162 thoracentesis for initial

pneumothorax and 1824 secondary pleural punctures for gas refills. Careful anesthetization of the needle tract with novocaine-adrenalin preceded all punctures. Primary punctures on the other hand were also supplemented by a subcutaneous injection of morphine, $\frac{1}{8}$ grain, as a sedative and the administration of sp. frumenti as a stimulant. The results of our analysis are shown in the accompanying table (page 840).

Scrutiny of this table discloses the fact that among the 162 primary punctures, pleuro-pulmonary reflex was encountered in 7 patients, in 3 of whom the attacks recurred on subsequent attempts to enter the pleural space. Three of these attacks were mild, 6 were severe, and 1 ended fatally. The most severe and outstanding symptom during the attacks was cardio-respiratory embarrassment. It was present in all. This distressing symptom was of the vago-inhibitory type in 3 and vasomotor in 7, the former being characterized by slowing of respiration and decreased frequency and increased force of the pulse, the latter by rapid, shallow and cessation of respiration, and rapid, feeble and ultimately imperceptible pulse and heart beat.

Unconsciousness was noted in 4, tonic and clonic muscular contractions in 5, and temporary paralysis in 7. Amblyopia was noted in 3 cases and loss of control of sphincters in 1. Precordial pain was severe in 4. *In 7 instances injury to the visceral pleura and underlying lung tissue undoubtedly occurred.* This was evidenced by frank hemopytsis or blood-streaked sputum immediately following the introduction of the needle. In 6 of these cases physical and roentgenological examinations disclosed the existence of extensive pleuro-pulmonary infiltration and fibrosis underlying the point of puncture, and our attempts to induce pneumothorax in these were unavailing.

On the other hand, among the 1824 punctures for refills, *i. e.*, thoracentesis performed in those cases wherein the pleural surfaces were widely separated from each other by pneumothorax so that the needle could not possibly injure the visceral pleura and underlying lung tissue, the accident occurred but twice. In 1 of these cases, on account of the rapid and unexpected reëxpansion of the compressed lung, the needle caused sufficient injury to result in frank hemoptysis, and in the other the cardio-respiratory embarrassment was of the vagotonic or inhibitory type and followed what appeared to be the separation of an adhesion.

Comment. Scrutiny of the clinical data reveals not only suggestive information but point to factors which have a definite etiological relation to pleuro-pulmonary reflex. Dayton,[30] in his excellent monograph on pleural reflex occurring in the course of ordinary exploratory thoracentesis, provides data which are both interesting and instructive. He found that in 17 of his 23 cases there was definite evidence that the visceral pleura had been

TABLE I.—SHOWING SYMPTOMATOLOGY IN GENERAL AND ESPECIALLY BLOOD STREAKED SPUTUM, INDICATING PLEURO-PULMONARY INJURY, IN 13 INSTANCES OF PLEUROPULMONARY REFLEX.

Name.	Side.	Puncture.	Onset of symptoms.	Unconsciousness.	Temporary paralysis.	Muscle contraction.	Cardio-respiratory failure.	Blood in sputum.	Remarks.	Extent of pneumothorax.
H. S.	Right	1st	Immediate	No	Right arm; left leg	General severe	Severe vasomotor	Streaked	Precordial pain; amblyopia	None.
H. S.	Right	2d	Immediate	Yes	Right arm; left leg	General severe	Severe vasomotor	Streaked	Amblyopia	None.
S. L.	Left	1st	Immediate	No	Both legs	Left arm	Vago-inhibitory	Streaked	Amblyopia	None.
M. S.	Left	20th	Immediate	Yes	Both legs	None	Vago-inhibitory	Hemoptysis	Disorientation	Fair.
A. K.	Left	2d	Immediate	No	None	None	Vago-inhibitory	Streaked	.....	Fair.
A. K.	Left	3d	Immediate	No	None	None	Vago-inhibitory	Streaked	.....	Fair.
I. A.	Left	1st	Immediate	Yes	Left leg	None	Vasomotor	Streaked	Precordial pain	None.
I. A.	Left	2d	Immediate	No	Left leg	None	Vasomotor	Streaked	Precordial pain	None.
B. D.	Left	1st	Immediate	No	None	None	Vasomotor	Streaked	Precordial pain	None.
B. D.	Left	5th	Immediate	Yes	None	Left leg	Severe vasomotor	Streaked	Died	None.
A. R.	Right	1st	Immediate	No	Right face	None	Vasomotor	None	Cardiac dilatation	None.
E. W.	Right	1st	Immediate	No	None	Right arm	Vasomotor	Streaked	Dyspnea	None.
J. B.	Right	1st	Immediate	No	None	None	Vasomotor	Streaked	Dyspnea	None.

pierced and the lung underneath injured. In over 75 per cent of these, most of which came to autopsy, the lung underlying the point of puncture was consolidated either on account of unresolved pneumonia, tuberculosis or compression. He concluded therefore, that pleural reflex is a result of the stimulation of the vagus nerve, probably in the visceral pleura and possibly in the lung and that accidents occur more often in cases with consolidation due to chronic inflammatory changes.

Saugman[31] has observed that the occurrence of pleural reflex in his wide practice has markedly decreased since he uses all known methods to avoid injury to the lung at the point of puncture.

Our own observations have brought out 4 significant points. (1) That in over 75 per cent of all cases of pleuro-pulmonary reflex there was definite evidence of injury to the visceral pleura and underlying lung tissue. (2) That in these cases the pleuro-pulmonary tissue underlying the point of puncture was the seat of pathological processes of an acute nature. (3) That pleuro-pulmonary reflex practically never followed thoracentesis when the two pleural surfaces were widely separated by induced pneumothorax so that the visceral pleura and lung tissue could not possibly be injured by the needle. (4) That puncture of the parietal pleura when anesthetic is used never causes symptoms ordinarily ascribed to this reflex.

Most of the data derived from experimental investigation are unfortunately vague and even misleading. We will therefore refer briefly only to the excellent investigations of Capps and Lewis which stand out in bold relief against the haze of hypotheses and theories concerning the nature of pleural reflex. These observers differ from Brodie and Russell in that they did obtain pleural reflexes on irritation of both healthy and inflamed pleural surfaces. They maintain that in dogs with induced pleurisy, excitation of the inflamed visceral pleura gives varied results. In some there is no marked change in the blood-pressure, while in others there is a considerable fall in the blood-pressure that may often be fatal. "These reflexes," they say, "conform to two types which, as a rule, occur singly but may be combined. (1) Cardio-inhibitory type, in which the heart is slowed and pulse tracings make violent excursions with great range between systolic and diastolic pressure. Respiration is slowed and inhibited. This type seldom proves fatal. (2) The vasomotor type, in which the pulse tracings show a steady, rapid decline, with no great difference in systolic and diastolic pressure, is frequently fatal. Respiration as a rule is shallow but may be rapid, and in fatal cases the abdominal viscera are much engorged from great vasodilatation. The brain shows no evidence of embolism or hemorrhages. The cardio-inhibitory reflex is central because it is prevented by cutting both vagi. Atropine doses paralyze the

cardio-inhibitory fibers and destroy the reflex. The vasomotor reflex may be central or peripheral. If central, they reach the medulla by the way of the thoracic sympathetic nerves and no vago-sympathetics. This is proved by failure of section of the vago-sympathetic cord to alter or abolish the reflex. If peripheral, the reflex goes from the pulmonary fibers to the pulmonary plexus, thence to the thoracic sympathetic nerve, downward to the splanchnic, and celiac plexuses in the abdomen. This reflex is more direct than the central form, but seems inconsistent with views generally accepted as to the cause and direction of impulses in the sympathetic nerve."

It is apparent therefore, that the clinical data above referred to are strongly supported by the results of the experimental investigations of Capps and Lewis, and it seems fair to assume that in many cases it is the injury to and irritation of the inflamed visceral pleura and underlying lung tissue that give rise to the symptom-complex now designated as pleuro-pulmonary reflex.

Methods of Prevention. In the light of our present conception of the etiology of this distressing reflex, it is apparent that definite measures can be taken in its prevention. Indeed, such measures have been taken by most skilled pneumothorax workers, who, like Saugman, have avoided unnecessary injury to the visceral pleura and underlying lung tissue.

It betrays a lack of familiarity with the literature on the subject to argue that cases of pleuro-pulmonary reflex are rare, and those who still maintain this view have either been extremely fortunate or have enjoyed a limited observation. To quote Dayton, "one sudden death is infinitely more convincing than many negative experiences."

A thorough consideration of the clinical history and physical findings will in numerous instances make an exploratory puncture unnecessary and thus prevent accidents, which for obvious reasons are particularly apt to occur in dry taps. The roentgen ray should be used in many doubtful cases in great preference to exploratory puncture. When there is a suspicion of the existence of a small effusion, a delay of a day or two to clear up the diagnosis will do no harm and recent developments in the treatment of empyema point to the fact that even in purulent exudates a little patience on the part of the operator is of unquestionable benefit to the patient.

When there is a definite indication for exploratory puncture, careful anesthetization of the entire needle tract, especially the deeper musculature and parietal pleura, should be carried out to avoid if possible those reflex impulses which may originate in it.

Most observers are in agreement with Saugman that it is only in exceptional cases that a needle longer than 3 cm. is necessary for thoracentesis. We frequently miss the exudate and injure the lung by going in too deep with the larger needles. Further-

more, experience shows that aspiration for diagnostic purposes can be done through the anesthetizing needle in all cases not excluding those in which the exudate is thick and cheesy. Added caution is to be exercised when fluid is not easily obtainable, for it is in dry taps that the chances of injuring the visceral pleura and underlying lung tissue are very great. The mesial portion of the chest should be avoided, even though great care is taken to prevent injury to the larger vessels, the pericardium and its contents, because, as has been shown by Brodie and Russell, injury to the larger nerve trunks at and near the hilus region may result in severe and even fatal accidents. Under no circumstances should the needle be moved laterally after it is inserted into the pleural cavity. Nor should the point of the needle be permitted to inscribe arcs of a circle within the thorax. Such manipulation offers sure means of injuring the lung and pleura. It is far safer, in searching for fluid, to make several punctures at different points in the chest than to move the needle in several directions from one point of puncture. It is important for reasons already recounted, to choose the point of puncture as far away from the inflamed pleuro-pulmonary tissue as possible, and in localized collections of fluid the roentgen ray will indicate the safest point to go into with a certainty far surpassing that of the most skilful diagnostician.

No less caution is to be exercised in the initial inflation in pneumothorax. Indeed, the chances for accident are even greater than in exploratory thoracentesis, because the visceral pleura and lung tissue, not being pushed away by fluid, can very readily be injured by the intruding needle. A point of puncture must be chosen as remote as possible from the main lesion and hilus region. Adhesions must be avoided. And while it is often possible to keep away from the site of the main lesion, no known method can definitely exclude the presence of adhesions at a certain point. Indeed, they are present where we least expect them and the roentgen ray often fails to point to their existence. As a rule, it is safest to go into an area giving a good, resonant note on percussion and fair breath sounds on auscultation; and while it is obvious that a free pleural space may easily be found in an area over which pleural friction sounds are audible, it is certain that punctures at such points are fraught with danger.

A short needle, not longer than 3 cm. and of narrow gauge should be used for anesthetizing purposes and the inflations should be given through the same needle. This can be accomplished in all cases presenting a free pleural space. In the past five years we have not failed to induce all our initial pneumothoraces with the anesthetizing needle. The use of a longer and wider caliber needle is not only unnecessary but distinctly dangerous, and that accidents with these needles are not more common than reported is due either to good fortune, or more probably to the disinclination on the part of their users to divulge.

The old practice of asking the patient to cough while the needle is in the chest cavity so as to augment the manometric oscillations is mentioned here only to be condemned. There is no surer way to injure the pleura and lung tissue.

A needle that is blocked can be made patent by the stilet, or by aspiration with a syringe which should at all times be connected to the pneumothorax needle.

TREATMENT. When symptoms pointing to pleuro-pulmonary reflex make their appearance, the needle should be forthwith withdrawn from the pleural cavity. When the cardiac embarrassment is of the vago-inhibitory type, reassurance of the patient and patience on the part of the operator are all that is necessary. Atropine, to counteract the vagus inhibition, may be administered subcutaneously in fair doses.

On the other hand, should the cardiac embarrassment be of the vasomotor type, adrenalin is urgently indicated and stimulation is at once to be resorted to. Hot coffee, per rectum, and camphor in ether subcutaneously have been strongly recommended. The vast majority of patients recover in from half an hour to one hour, although amblyopia and temporary paralysis may persist for several hours. These however, leave no permanent defects. The patient should remain in bed for a few days or until such time when all symptoms due to the reflex phenomena have disappeared.

It is pertinent to mention that inasmuch as pleuro-pulmonary reflex has a tendency to repeat itself in subsequent pleural punctures for the induction of pneumothorax, most operators are in entire accord with Forlanini who deems it advisable to abandon this form of therapy when the accident occurs with each of the first two attempts to enter the pleural space. Failure to heed this warning may and actually has entailed sad consequences.

Summary. 1. Pleuro-pulmonary shock or reflex may occur with amazing and dramatic suddenness in the course of ordinary exploratory thoracentesis and pleural puncture for the induction of therapeutic pneumothorax.

2. The most constant and distressing feature of this symptom-complex is cardio-respiratory failure. Among other outstanding symptoms are tonic and clonic contraction of the body musculature, amblyopia, temporary paralysis of various parts of the body, and loss of consciousness. Severe cases may end fatally.

3. The cardio-respiratory failure may be of (*a*) the cardio-inhibitory type in which the heart is slowed and the pulse is slow and forceful, with great range between systolic and diastolic pressures, and the respiration greatly inhibited; (*b*) the vasomotor type (the more dangerous) in which the pulse becomes rapid, feeble and imperceptible and respiration is shallow and hurried, and (*c*) a combination of the two types.

4. Clinical and experimental evidence lead us to believe that

injury to the inflamed visceral pleura and lung tissue underlying the point of puncture is a definite factor in the causation of this distressing symptom-complex. It is for this reason that thoracentesis in cases with copious pleural effusion or extensive pneumothorax, that is, punctures in cases where the lung tissue and visceral pleura, on account of their position, cannot be injured by the intruding needle, are rarely if every followed by this accident.

5. Attempts at pleural aspiration in doubtful cases and punctures for initial pneumothorax, because of the fact that the inflamed visceral pleura and lung tissue immediately underlie the point of puncture, should be made with the greatest caution, as it is in such cases that this symptom-complex is most liable to occur.

6. Pleural punctures in such cases should be made as far away as possible from the site of the main lesion. The needle should be of small caliber, held firmly and prevented from moving within the chest cavity. It is safer in order to avoid injury to the visceral pleura to make several punctures at different points on the chest wall than to move the needle in several directions from one point of puncture.

7. In hospital practice it is far safer in cases of doubtful or localized pleural effusions to depend on the roentgenological examinations which will indicate the presence of such effusions with an accuracy far surpassing that of the most skilful diagnostician. This applies to purulent as well as serous effusions.

8. When symptoms pointing to the reflex make their appearance, the needle should be at once withdrawn. If the cardio-respiratory failure is of the cardio-inhibitory type, reassurance of the patient and a little patience on the part of the physician is all that is necessary, although atropine may be given subcutaneously in severe cases, none of which however, have proven fatal. If the cardio-respiratory failure is of the vasomotor type, adrenalin should at once be given subcutaneously and stimulation should be resorted to. Hot coffee, per rectum, caffein and camphor subcutaneously have been found most useful. The temporary paralysis and amblyopia as a rule clear up completely within a few days and require no special treatment.

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STUDIES IN RENAL FUNCTION AND METABOLISM IN A CASE OF DIABETES INSIPIDUS.

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Diabetes insipidus is a disease concerning the etiology of which we are still largely in the dark. That it bears some relation to disturbed pituitary function seems probable, yet much remains to be done to elucidate the relationship.

During the course of a study of a case of diabetes insipidus admitted to the medical wards of the Cincinnati General Hospital, several unusual findings were made concerning the renal function, blood chemistry and the metabolism of the individual. It was thought wise to report these findings in a further endeavor to aid in determining the principles underlying the cause of the polyuria.

The effect of pituitary extract (posterior lobe) in reducing the urinary output in cases of diabetes insipidus was again demonstrated, as well as its ability to concentrate the urine. A study of the antidiuretic effect of pituitary extract upon other conditions producing polyuria, such as chronic interstitial nephritis and diabetes mellitus, is now in progress.

A review of the subject will be dispensed with because excellent reviews are to be found in the Oxford Medicine,[1] in articles by Barker and Mosenthal,[2] Rabinowitch,[3] and Weir, Larson, and Rowntree.[4]

CASE REPORT.—*Chief Complaint.* A male, white boy, aged twelve years, was admitted December 26, 1921, to the service of Dr. Roger S. Morris, complaining of "water diabetes."

Family History. The family history is essentially negative.

Previous History. Patient had scarlet fever one year ago; the exact time and duration of the disease was not known. Immediately following this, he developed a polyuria.

Present Illness. For the past year the patient had been voiding as frequently as twelve to fifteen times during the day and four to five times during the night. The quantity of urine voided each time was about a pint. There had been no burning upon micturition. He said that frequently there was a feeling of discomfort over the bladder region just before voiding. At times he would become quite thirsty and would void soon after the intake of water. Enuresis was a common occurrence. His appetite was moderate and there had been no loss of weight during the past year.

Physical Examination. Examination made by Dr. Morris revealed a fairly well developed and nourished boy lying quietly in bed. The complexion was fair. Hair was blonde; the texture was fine. No deformities of the head. The skin was soft and clear. There was no abnormal growth of the body hair for a boy of this age. The posterior chain of cervical glands was felt. Epitrochlear glands were palpable. The heart, lungs, and abdomen were normal. The reflexes were equal and active. Blood-pressure: Systolic, 95; diastolic, 55.

Routine Laboratory Record. Blood. Wassermann was negative. Red blood cells, 4,020,000; leukocytes, 11,200; hemoglobin, 80 per cent (Sahli). Differential count: Polymorphonuclear neutrophiles, 61.5 per cent; lymphocytes, 33.5 per cent; eosinophiles, 1 per cent; large mononuclears and transitionals, 3 per cent; unclassified, 1 per cent.

Urine. Clear, pale, acid reaction, no sediment, specific gravity 1.003, microscopical examination negative. Patient voided almost hourly in amounts ranging from 300 to 500 cc. The daily twenty-four hour urinary output ranged between 3 and 9 liters; accurate records could not be kept because patient voided involuntarily during the night. The specific gravity was fixed ranging between 1.001 and 1.003 during the twenty-four hour period. The relationship between the individual voidings and the specific gravity is shown in Fig. 1.

Roentgenogram of Skull. Stereoscopic plates of the skull made with the left side down showed no abnormalities. The sella turcica was slightly shallow.

Treatment. The value of the administration of posterior lobe pituitary extract in cases of diabetes insipidus being known, as demonstrated by R. von den Velden, the patient was started on

the dried extract. Increasing doses of the salol coated and non-coated pills up to 3 grains, three times daily failed to produce the desired effect. The intramuscular injection method was then resorted to with immediate and striking results. One cc of obstetrical pituitrin* injected intramuscularly relieved the thirst and decreased the polyuria (Fig. 2). The effects of the extract were noted within ten minutes and lasted over a period of eight to ten hours. The action of the drug in concentrating the urine, its effect on the phthalein output, blood chemistry and basal metabolism will now be considered in detail.

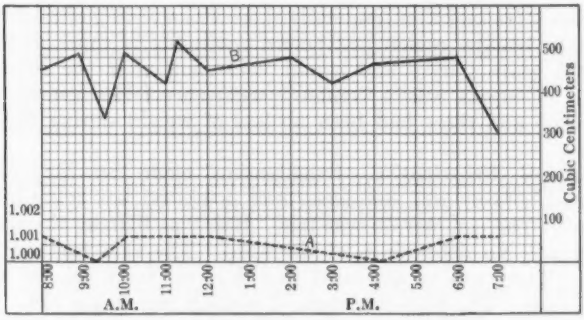

FIG. 1.—A chart showing the specific gravity and individual voidings of a typical twenty-four-hour period before the administration of pituitrin in any form. Note (Curve A) the very low and constant specific gravity.

THE EFFECT OF PITUITRIN ON THE URINARY SECRETION. During his stay in the hospital, the patient was kept on the regular hospital diet. Water was allowed as desired. In Table I is given the volume, specific gravity, chloride and urea nitrogen concentration during a twenty-four hour period.† It will be seen that the patient voided 8,610 cc of urine during twenty-four hours, the quantities voided ranged between 300 and 510 cc. The specific gravity varied between 1.002 and 1.010, the maximum of salt concentration was only 0.165 per cent and that of the urea nitrogen was 0.08 per cent. The total grams of salt secreted was 10 and the total grams of urea nitrogen secreted was 5.88, both of which were normal for the patient under the diet given. Fig. 3 is a graphic representation of the essential features shown in Table I.

In Table II are given the volume, specific gravity, salt, and urea nitrogen concentrations of a twenty-four hour period during which the patient had received 2 cc of obstetrical pituitrin intra-

* An aqueous extract of the posterior lobe of the pituitary prepared by Parke, Davis & Co. for obstetrical use.

† The sodium chloride was determined by the Vollhard principle, and the urea nitrogen by the direct Nesslerization method of Folin. During this period the patient received the dried extract of pituitary gland by mouth.

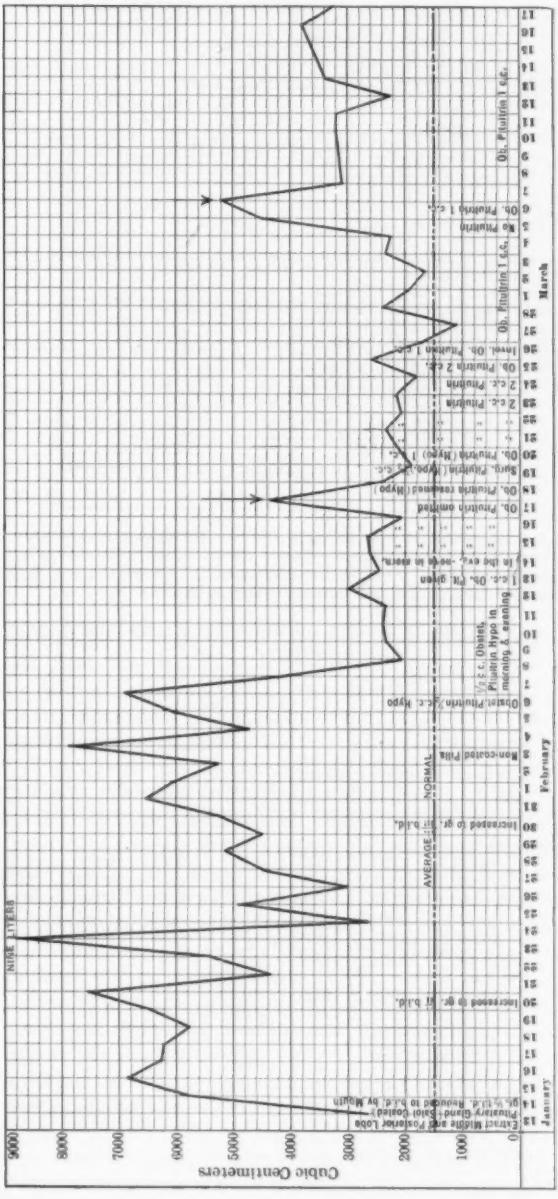
Cubic Centimeters
NINE LITERS
AVERAGE
NORMAL
Extract Middle and Posterior Lobe Pituitary Gland (Solid Gelatin) 0.5 c.c. Reduced to 0.1 c.c. By Mouth
Increased to gr. ½ b.i.d.
Increased to gr. ¼ b.i.d.
Non-coated Pills
Distal. Pituitrin 1 c.c. Hypo
½ c.c. Obstet. Pituitrin Hypo in morning & evening
1 c.c. Op. Fld. given in the eve., none in morn.
Op. Pituitrin omitted
Op. Pituitrin restored (Hypo.)
Surg. Pituitrin (Hypo.) 1 c.c.
Op. Pituitrin (Hypo.) 1 c.c.
2 c.c. Pituitrin
2 c.c. Pituitrin
Op. Pituitrin 2 c.c.
Interl. Op. Pituitrin 1 c.c.
Op. Pituitrin 1 c.c.
No Pituitrin
Op. Pituitrin 1 c.c.
Op. Pituitrin 1 c.c.
January
February
March

FIG. 2.—A curve showing the daily urinary output over a period of sixty-four days. Note the ineffectiveness of pituitary extract given in various forms by mouth and the marked drop in the urinary output immediately following the hypodermic injections of pituitrin. The arrows point to the increase of the urinary output on two occasions, both of which were due to the temporary omittance of the pituitrin. Note that 1 to 2 cc of the pituitrin had to be given daily to control the polyuria.

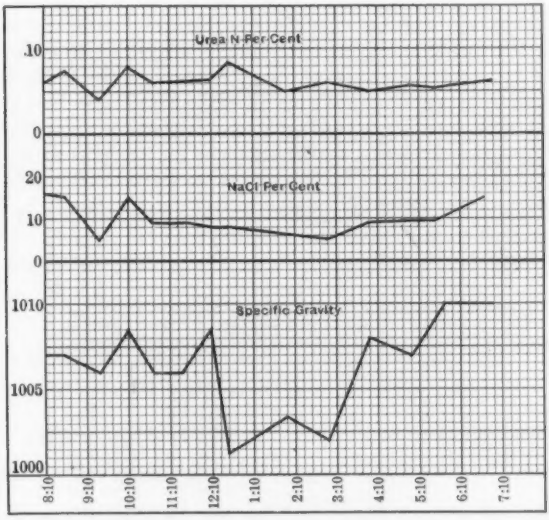

FIG. 3.—Curves showing the urea nitrogen and salt percentage and the specific gravity of individual specimens of urine collected during a twenty-four-hour period before the administration of pituitrin hypodermatically. Note the low specific gravity and the low chloride and urea nitrogen percentages.

TABLE I.—ANALYSES OF URINE DURING ORAL ADMINISTRATION OF PITUITRIN.

No.	Time.	Urine.					
		Volume. S.T.	Specific gravity.	NaCl.		Urea nitrogen.	
				Per cent.	Grams.	Per cent.	Grams.
	A.M.						
1	8.10	450	1.007	0.165	0.74	0.060	0.27
2	8.40	480	1.007	0.150	0.72	0.070	0.34
3	9.30	360	1.006	0.045	0.16	0.045	0.16
4	10.10	480	1.008	0.150	0.72	0.080	0.38
5	10.50	420	1.006	0.090	0.38	0.070	0.29
6	11.15	510	1.006	0.090	0.46	0.070	0.36
	P.M.						
7	12.10	450	1.008	0.070	0.31	0.070	0.32
8	1.30	480	1.001	0.070	0.34	0.080	0.38
9	2.00	480	1.003	0.056	0.27	0.050	0.24
10	3.00	420	1.002	0.045	0.18	0.070	0.29
11	4.00	480	1.008	0.090	0.43	0.050	0.24
12	5.00	480	1.006	0.090	0.43	0.060	0.29
13	5.35	480	1.010	0.090	0.43	0.050	0.24
14	7.00	300	1.010	0.150	0.45	0.070	0.21
Total day	....	6270	....	....	6.02	....	4.01
7 P.M. to 7 A.M.	....	2340	1.007	0.170	3.98	0.080	1.87
Total	24 hours	8610	....	....	10.00	....	5.88

TABLE II.—ANALYSES OF URINE FOLLOWING ADMINISTRATION OF 2 CC OBSTETRICAL PITUITRIN HYPO.

No.	Time.	Quanitative urine analysis.					
		Volume. Cc.	Specific gravity.	NaCl.		Urea nitrogen.	
				Per cent.	Grams.	Per cent.	Grams.
	A.M.						
1	7.30	280	1.005	0.165	0.462	0.050	0.140
2	8.50	220	1.004	0.115	0.253	0.054	0.119
3	10.00	200	1.014	0.340	0.680	0.360	0.720
4	11.10	260	1.014	0.650	1.690	0.208	0.541
	P.M.						
5	1.00	300	1.012	0.335	1.005	0.375	1.125
6	2.10	300	1.008	0.160	0.480	0.190	0.570
7	3.00	240	1.007	0.145	0.348	0.125	0.300
8	4.30	200	1.007	0.175	0.350	0.111	0.222
9	6.30	300	1.009	0.155	0.465	0.133	0.399
10	7.10	200	1.006	0.150	0.300	0.077	0.154
Total day	....	2500	....	....	6.033	....	4.290
7.10 P.M. to 7 A.M.		1000	....	0.200	2.000	0.272	2.720
Total	24 hours	3500	....	....	8.033	....	7.010

One cubic centimeter of pituitrin intramuscularly at 8 A.M. and 8 P.M.

muscularly; 1 cc at 8 A.M. and the other cc at 8 P.M. It will be seen that the patient voided 3500 cc during twenty-four hours; the quantities voided ranged between 200 and 300 cc; the specific gravity varied between 1.004 and 1.014, the maximum of salt concentration was 0.650 per cent and that of the urea nitrogen was 0.375 per cent. The total number of grams of salt secreted was 8.033, and that of the urea nitrogen was 7.010. Fig. 4 is a graphic representation of the essential features presented in Table II. Curves are drawn illustrating the variations in the urea nitrogen and salt concentration and the specific gravity from hour to hour. It will be seen that the maximum height of the urea nitrogen, the salt concentration and the specific gravity curve was reached approximately between two and three hours following the intra-muscular injection of 1 cc of pituitrin.

Summary. From these findings it is justifiable to conclude, that in some obscure way pituitrin has the power of concentrating the urine. As shown, both in Table II and in Fig. 4 the maximum of concentration, as indicated by the specific gravity, salt and urea nitrogen percentages, is reached approximately between two and three hours after the intramuscular injection of 1 cc of pituitrin. The specific gravity curve approaches the normal, showing a variation of ten points during the day.

THE EFFECT OF PITUITRIN UPON THE PHTHALEIN OUTPUT. A further study of renal function was then made by means of the phthalein test of Rowntree and Geraghty. The phthalein test performed a few days after admission showed an excretion of only 26 per cent of the dye in two hours; 18 per cent the first hour; 8

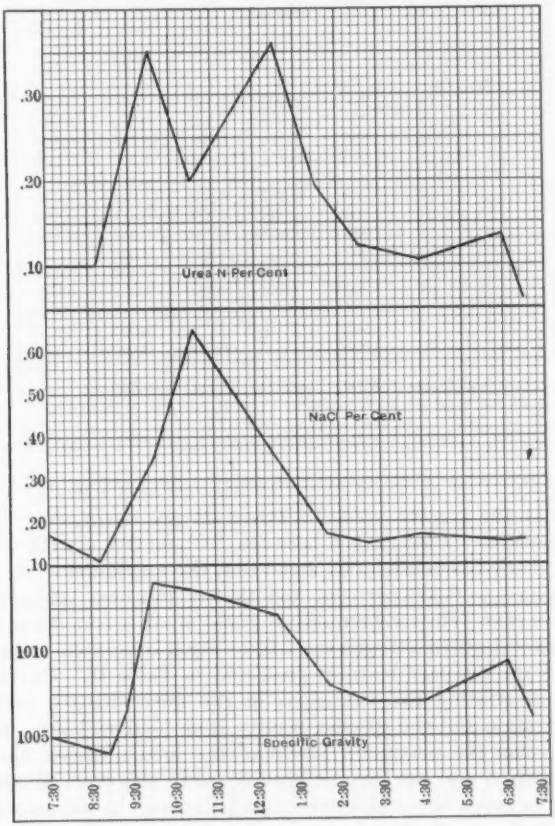

FIG. 4.—Note the rise in the specific gravity and the urea nitrogen and salt percentages. Maximum rise occurred about three hours after 1 cc of pituitrin was given hypodermatically.

per cent the second hour. A few days later, a second phthalein test showed an excretion of 36 per cent of the dye in two hours; 31 per cent the first hour and 5 per cent the second hour.

A similar test was performed during the course of treatment as follows: The patient was given 1 cc of pituitrin intramuscularly at 7.45 A.M. followed by 2 glasses of water. At 8.00 A.M. (fifteen

minutes later) 1 cc of phenolsulphonephthalein was administered intramuscularly. The urine passed was collected for the first hour and second hour respectively. Forty-two per cent of the dye was excreted during the first hour and 17 per cent during the second hour or a total of 59 per cent in two hours.

The pituitrin was then discontinued. Thirty-six hours later another phthalein test was performed showing an excretion of 40 per cent of the dye in two hours; 28 per cent the first hour and 12 per cent the second hour. These findings are graphically shown in Fig. 5.

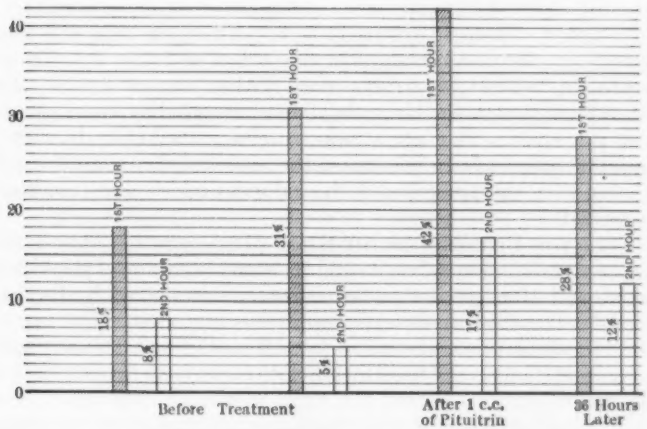

FIG. 5.—Note the increase in the phthalein output immediately following the injection of pituitrin and then the decrease after thirty-six hours of abstinence from the drug.

Summary. From these results one may conclude that pituitrin has not only produced an increase in the salt and urea nitrogen concentration of the urine, but also an increase in the phenolsulphonephthalein output. Thus it is evident that the secretion of the dye and that of the salt and urea are more or less parallel in nature in this case of diabetes insipidus.

EFFECT OF PITUITRIN ON THE BLOOD CHEMISTRY. Blood analyses* were made before and after the administration of pituitrin intramuscularly. Before treatment the blood analysis was as follows:

	Mg. per 100 cc of blood.
Sugar	87.0
Urea nitrogen	8.3
Uric acid	1.8
Chlorides	515.0

* The blood constituents were determined by the system of Folin and Wu.[7] The blood chlorides were determined by the method of Whitehorn.[8]

A specimen of blood was then taken three hours after the injection of 1 cc of pituitrin intramuscularly. This time was selected because it was shown that urine of maximum concentration (Table II and Fig. 4) was excreted between two and three hours after the intramuscular injection of the pituitrin. The analysis of this blood was as follows:†

	Mg. per 100 cc of blood.
Sugar	111.0
Urea nitrogen	16.0
Uric acid	3.5
Chlorides	370.0

Summary. Thus it will be seen that, although there was some variation in the blood chemical picture before and after the pituitrin treatment, all of the figures were within normal limits. The blood findings were similar in the 15 cases reported by Weir, Larson, and Rowntree.[4] But upon more careful examination it will be seen that there was an increase in the concentration of all the substances with the exception of the chlorides which were markedly decreased.

Effect of Pituitrin on the Basal Metabolism. The relation between the basal metabolism and the water excretion of the kidney before and after pituitary administration was studied by Raphael Isaacs. The Sanborn-Benedict apparatus was used. The normal oxygen consumption was taken from Benedict and Talbot's table for normal standards of basal metabolism for boys and girls.[6] Before any treatment was started the basal metabolic rate was −5 per cent. After a month of the administration of pituitary substance in coated and non-coated pills by mouth the rate was −5.68 per cent. After six weeks, during which time the pituitrin was given hypodermatically, the basal metabolic rate was −1.9 per cent twelve hours after the injection of 1 cc of pituitrin. Then 1 cc of pituitrin was given. Forty-five minutes later, the basal metabolic rate was + 1.3 per cent. The calculated urinary output, the vital capacity, and the respiratory and pulse rates were as follows:

TABLE III.

	Before pituitrin.	After pituitrin.
Basal metabolic rate	−1.9 per cent	+1.3 per cent
Urinary output	800 cc per hour	75 cc per hour
Vital capacity	2350 cc	2250 cc
Respiratory rate	14 per minute	16 per minute
Pulse rate	76 per minute	80 per minute

† On this examination, non-protein nitrogen and creatinine determinations were also made with the following results: Non-protein nitrogen, 35.3 mg. per 100 cc of blood; creatinine, 1.5 mg. per 100 cc of blood.

Summary. It will be noted that, although the water output dropped from 800 cc to 75 cc per hour, there was scarcely any perceptible change in the basal metabolic rate. Two interpretations are possible. Either the excretion of water by the kidney does not involve "work" and the consumption of oxygen, or else the decreased oxygen consumption resulting from the lessened urinary output was compensated for by increased oxidations elsewhere.

Conclusions. 1. Two cc of obstetrical pituitrin, administered intramuscularly during a twenty-four hour period decreased the polyuria in a case of diabetes insipidus. The specific gravity was raised and the percentage of salt and urea nitrogen was increased. The maximum concentration was reached within three hours after the injection of the pituitrin. The drug produced its effect immediately (within ten minutes) and was only transient in its action; the effect of 1 cc lasting from eight to twelve hours.

2. Pituitrin injected hypodermatically enabled the kidney to excrete a larger amount of phenolsulphonephthalein.

3. The concentration of the urea nitrogen, uric acid, and sugar in the blood was almost doubled within three hours after the injection of 1 cc of pituitrin. The blood figures before and after injection of the pituitrin remained within normal limits.

4. There was no apparent relation between the basal metabolism and the water excretion of the kidney before and after pituitrin administration.*

* The writer wishes to thank Drs. Cecil Striker, Joseph Ganim, Floyd Hendrickson and Miss Agnes Wolfstein for their help in the completion of this case. He is deeply indebted to Dr. Roger S. Morris for his many suggestions and the privilege of reporting this case.

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SPLENIC ANEMIA: A CLINICAL AND PATHOLOGICAL STUDY OF SIXTY-NINE CASES.*

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Osler, in his *Principles and Practice of Medicine*, discusses splenic anemia under the heading, "Primary Splenomegaly with Anemia," which he defines as "a primary disease of the spleen of unknown origin, characterized by progressve enlargement, attacks of anemia, a tendency to hemorrhage, and in some cases a secondary cirrhosis of the liver, with jaundice and ascites. That the spleen itself is the seat of the disease is shown by the fact that complete recovery follows its removal." Osler has included the cases of primary splenomegaly which Rolleston prefers to discuss under separate headings, "Chronic Splenic Anemia" and "Banti's Disease."

According to Rolleston, chronic splenic anemia presents the following characteristics: "(1) Chronic splenomegaly which cannot be correlated with any recognized cause; (2) the absence of enlargement of the lymphatic glands; (3) chronic anemia (with low color index); (4) the absence of leukocytosis and usually the presence of leucopenia; (5) liability of copious gastro-intestinal hemorrhages from time to time; and (6) prolonged course without any tendency to spontaneous cure, though splenectomy is usually curative."

Rolleston, in discussing the relation between Banti's disease and splenic anemia, says, "The title, Banti's disease, is now often used as synonymous with splenic anemia even by those who fully recognize that it is a sequel or terminal stage of splenic anemia and does not occur in all cases even when unduly prolonged."

According to Hollins, Banti describes three stages of the disease named for him: (1) the preascitic stage in which splenic enlargement is present with or without anemia; (2) the transitional stage of which the most prominent symptom is diarrhea; anemia and blood changes are found, the liver is somewhat enlarged, and jaundice may be present, and (3) the ascitic stage, or Banti's disease proper.

This report is the result of a study of the pathological findings and clinical records of 69 patients with splenic anemia, on whom splenectomy was performed at the Mayo Clinic from November 14, 1905, to September 1, 1920. Patients who had a distinct hepatic cirrhosis in addition are also considered.

* Abridgment of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Medicine.

The Microscopical Pathology. *Variation in the Normal Spleen.* Before the abnormality of any organ can be correctly investigated, it is essential that the pathologist have a clear conception of the normal. This is especially true in the case of the spleen, for the gross and microscopic picture may vary widely under normal conditions. Such normal changes may be permanent or temporary, as in variations with age or after severe hemorrhage or sepsis. Before the pathological study of splenic anemia was undertaken, therefore, an effort was made to learn of some of the variations that could be ascribed to normal influences.

Terminology. By *sinus endothelium* is meant a specialized form of endothelium and not the lining cells of blood channels as the term is commonly employed. These specialized endothelial cells of the sinuses are probably reticular cells and to be correct should be so designated. The word *pulp* is used to designate the cellular structures lying between the sinuses. *Pulp cords* would probably have been a more suitable term. *Reticulum* refers to all the connective tissue not included in the capsule, trabeculæ, or blood-vessels. Hyaline changes in the capsule and trabeculæ are not included under the term *degeneration* which is reserved for degenerative changes in the reticulum, in the malpighian corpuscles, or within the pulp.

Method of Study. In order to express more accurately the degree of pathological change observed in the study of the spleen, figures instead of descriptive adjectives, have been used. Normal findings were marked zero or simply normal. The degree of increase of the various processes above normal was designated on a scale +1, +2, +3, +4, while the decrease was graded −1, −2, −3, −4; +5 and −5 have been used occasionally in grading very unusual and extreme conditions.

At least three blocks of tissue were taken from each spleen, one containing a portion of the capsule of the diaphragmatic surface, one from near the center of the organ, and one from near the hilus. The last block always included a portion of the wall of one of the large veins.

Microscopical sections were made by the frozen-section method, or by embedding the tissue in paraffin. The routine stain was hematoxylin and eosin, but many of the specimens were also prepared with Dominici's and with methyl-green pyronin stains.

Microscopical Findings. A composite picture of the histo-pathology of splenic anemia is one of generalized fibrosis. There are no very definite and well defined characteristics which will enable the pathologist to say with certainty that the picture is one of splenic anemia (Fig. 1).

The wide variation in the pathological findings in splenic anemia has been one of the arguments used in an attempt to prove that cases so classified belong in closely related clinical groups and do

not bear a sufficient clinical and pathological resemblance to justify their being considered as distinct disease entities. From the pathological standpoint, in the case of the spleen, this argument is unfounded, for, while the pathological variations are great, the microscopical and gross studies give results probably as characteristic of splenic anemia as similar studies in the other groups of splenomegaly that present an accepted clinical syndrome, such as pernicious anemia, and hemolytic jaundice.

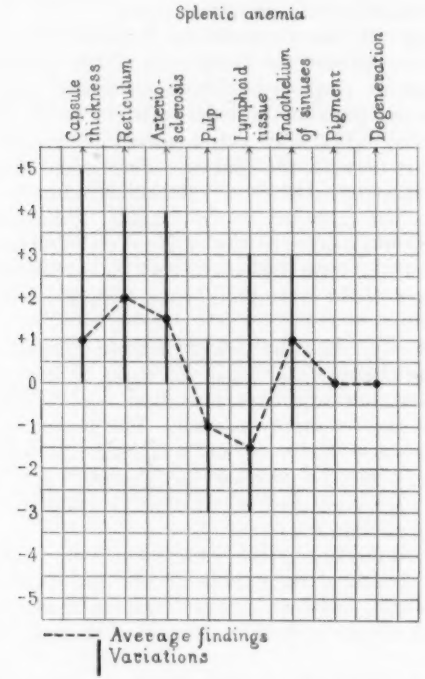

FIG. 1.—Average findings and the variations in the microscopical pathology of splenic anemia.

A great deal of the trouble in distinguishing, microscopically, splenic anemia from the other splenomegalies is owing to the variations encountered in the individual types of splenomegaly. In splenic anemia these variations were found to be quite marked. For example, the thickness of the capsule varied from normal to +5, the reticulum and the arterial walls from normal to +4, the pulp from −3 to +1, the lymphoid tissue from −3 to +3, and the endothelium of the sinuses from −1 to +3. While these variations are great, they are not surprising in view of the factors

that may influence the spleen, such as the duration and severity of the disease, the age of the patient, and the changes that may have been caused by previous diseases. These variations, while confusing, nevertheless suggest that the spleen plays an important part in the vital economy of the individual.

The average thickness of the capsule was found to be +1. The variation from +3 to +5 was caused by the extensive hyaline plaques in some of the spleens. For the most part, however, the thickness of the capsule in any given specimen was uniform. As a rule, the more fibrous the capsule the more prominent were the trabeculæ throughout the splenic tissue. Lymphocytic infiltration of the capsule was not seen in any of the sections.

The reticulum may be distinctly prominent either because of marked fibrosis or great cellular activity. The degree of fibrosis of the reticulum seemed to vary in a slight degree with the amount of thickening of the vessel walls, yet many cases were found in which the reticulum was very cellular and the degree of arteriosclerosis marked. The amount of lymphoid tissue present usually varied inversely to the prominence of the reticulum. The average amount of reticulum was found to be +2.

In the study of the degree of arteriosclerosis the artery of the malpighian corpuscle was chosen. It was observed that the more marked the arteriosclerosis, the greater the tortuosity of the vessel, so that it was often found that a malpighian corpuscle might show two to four cross-sections of the same artery. Marked arteriosclerosis was not necessarily associated with extensive fibrosis, and no evidence was found to suggest that fibrosis developed from the vessel wall. Indeed, marked fibrosis was often found in which the fibrous tissue was conspicuously absent in the region of the malpighian corpuscle and the central artery. Arteriosclerosis was, to a slight degree, an exception to the rule that in any given spleen the pathological changes were uniformly distributed. A few spleens showed a variation of from +1 to +3 in the degree of arteriosclerosis in various sections of the organ.

The artery of the malpighian corpuscle was in almost every case eccentrically located, and its position was apparently not disturbed by the thickening process of the vessel wall. There seemed to be at least one factor which helped to determine the size of the malpighian corpuscles, that is, encroaching fibrosis. The fibrosis, in turn, seemed to affect the position of the central artery by reducing, in an irregular fashion, the size of the malpighian corpuscle. It was a fairly constant finding that the greater the fibrosis the more eccentrically located was the artery. The average degree of arteriosclerosis was +1.5.

The degree of thickening of the arterial walls in cases of splenic anemia and in other types of splenomegaly were, syphilis +3, hemolytic jaundice +3, pernicious anemia +2, myelogenous leukemia +2, and splenic anemia +1.5.

No marked abnormality could be detected in the splenic veins, but the veins were usually so closely associated with the trabeculæ that a comparison of their walls was very difficult. In many cases, however, distinct hyaline changes were seen in the walls of the veins, but in no specimen was thrombophlebitis present.

In a spleen in which generalized fibrosis is a prominent feature, it would naturally be supposed that the amount of splenic pulp would be decreased. This was found to be true, and the average was +1. In general, the amount of splenic pulp varied inversely to the degree of fibrosis and the prominence of the sinuses. The proliferative activity of the endothelium of the sinuses, or the true reticular cells, was above normal and was rated +1. In nearly all the microscopical specimens the sinuses were prominent and dilated, but the other types of splenomegaly also showed it. The syphilitic spleens especially resembled those of splenic anemia in this particular. The prominence of the sinuses in splenic anemia averaged approximately +2.

The sinus endothelium or reticulum showed varying degrees of proliferation. In some specimens the cells seemed especially inactive, while in others the cells were very large and, as further evidence of activity, were free within the sinuses.

Downey, in an unpublished article, "The Structure and Origin of Lymph Sinuses of Mammalian Lymph Nodes" makes some very interesting statements: "Both the embryological and anatomical studies have shown, therefore, that the tissue of the splenic sinuses is to be regarded as reticulum rather than endothelium. . . . It is not identical with the endothelium of blood- and lymph vessels." With regard to the relation of the reticular tissue to the sinuses, he says, "The sinuses are closely associated with the reticular tissue of the organs concerned."

The amount of lymphoid tissue was found in many cases to be markedly below normal, but the average was estimated at −1.5. In determining the amount present in any given microscopical specimen, the malpighian corpuscles, perivascular lymphocytic infiltration, and the lymphocytes generally distributed throughout were considered. As a rule, the malpighian corpuscles were fairly well defined and small, but they did not stand out prominently nor were they seen often. Contrary to the findings of certain observers, in this series the so-called germinal centers were very rarely seen and, when found, were small and inconspicious. The intermediate zone of the malpighian corpuscle, "the zone of expansion" which in normal splenic tissue stains deeply and is prominent, was poorly defined and scarcely noticeable.

An attempt was made to study the minute capillaries which are connected with the splenic sinuses (Figs. 2 and 3). In normal splenic tissue these small blood channels consist of but a single layer of endothelial cells, the media and the adventitia disappear-

ing as the vessel approaches the size of a capillary. In splenic anemia and in the other splenomegalies, the spleens showed an increase of fibrous tissue around these vessel walls. Due allowance, however, must be made for the fact that the venules enter

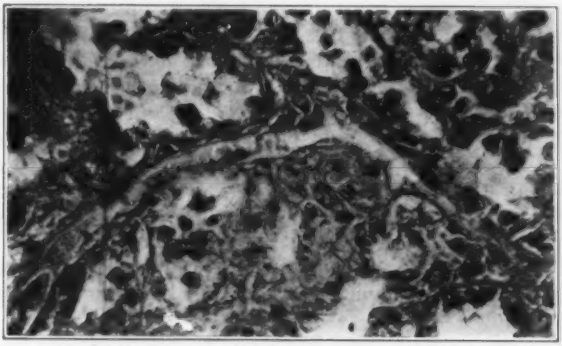

FIG. 2.—Splenic anemia; a capillary is seen.

the trabeculæ soon after their formation. In many instances the walls of these vessels showed a decided hyaline change so that the lumen became quite small and irregular.

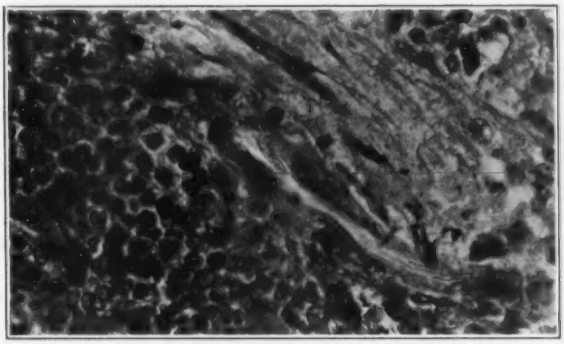

FIG. 3.—Splenic anemia; small capillary near a trabeculum.

In attempting to make a differential diagnosis of the various groups of splenomegaly the greatest difficulty was experienced with syphilitic spleens which resembled those of splenic anemia very closely. The sinuses in the syphilitic spleens were as prominent as those in the spleens of splenic anemia and the fibrosis was as great.

On account of the relative prominence of the malpighian corpuscles and the accuracy with which they can be studied, they were given special consideration, particularly from the standpoint of relative size and number, and general structure. While the malpighian bodies of splenic anemia were fairly prominent in the miscroscopical specimen, and were well circumscribed, they were not so prominent as in the normal, or in cases of pernicious anemia. There were only two or three specimens, however, in which the boundaries of the corpuscles could not be marked out with a fair degree of accuracy.

Contrary to many reports on the subject of splenic anemia, areas of degeneration or fibrous nodules were not found within the malpighian corpuscles. This, however, is entirely in accord with the ideas of Cushing and MacCallum who, in discussing splenic anemia, said, "No progressive sclerotic process, such as Banti described, is seen in these malpighian bodies nor has it been possible to find any fibrous nodules which might have resulted from such a sclerosis."

The larger the malpighian corpuscle, the greater was its tendency to be round or oval in shape and the nearer the center the artery seemed to be. As the generalized fibrosis increased in amount the malpighian corpuscles became smaller and were more irregular in outline.

As the fibrous tissue encroached on the periphery of the malpighian body, it seemed to cut off groups of cells somewhat irregularly. A continuance of this process resulted many times in the malpighian body being composed of a group of cells without a perceptible central artery, the vessel lying entirely outside of the corpuscle.

Before discussing the size of the malpighian body in splenic anemia the size of the normal should be considered. Gray gives the size of the malpighian corpuscles of the spleen as varying from 0.25 to 1 mm. in diameter. Morris gives the average size of the normal as 0.25 to 1.5 mm. Mall says the splenic lobule in a normal spleen is about 1 mm. in diameter and adds, "The malpighian corpuscle usually lies in the proximal end of the lobule, but in case it is very large it may distend the lobule and cause it to bulge."

In order to determine the size of the malpighian corpuscle in splenic anemia a camera lucida was used with the low power of the microscope (Fig. 4). Most of the corpuscles were not exactly round and for this reason the length and breadth were measured and the average was taken. When due allowance had been made for the magnification, it was found that the average size of the malpighian corpuscle was approximately 0.35 mm. in diameter. The variation in size was from 0.2 to 0.6 mm. It is evident, therefore, that the size of the corpuscles in splenic anemia is within the limits of normal, but that the average size is much below the average in the normal.

The next step was the determination of the number of malpighian bodies in a given area of splenic tissue in splenic anemia. The dissecting microscope proved to be very helpful in this work. A square 0.5 by 0.5 cm. was the size of the field chosen and three fields were counted in each spleen in order to get a general average of different portions of the organ. After determining the average for each spleen, the average for 69 spleens was found. The average number of malpighian bodies for each 0.5 cm. squared, or for $\frac{1}{4}$ of 1 sq. cm., was found to be nearly 6. The number of malpighian bodies in a square centimeter was estimated as approximately 23.

FIG. 4.—A malpighian corpuscle with a great amount of fibrosis around it. The central artery is cut obliquely.

Certainly this number is far less than the number of malpighian corpuscles in the same area in a normal spleen. In a series of about 12 normal spleens (far too few for calculating accurate averages), the number of malpighian bodies for each square centimeter was approximately 40.

The relation of the number of malpighian bodies to the size and weight of the spleens furnishes interesting data. As in all statements concerning the pathology of splenic anemia, however, there are many exceptions. The number of malpighian corpuscles to each square area seemed to decrease as the size and weight of the

spleen increased. The size of the malpighian body became smaller as the weight and size of the spleen increased. This was found to be true in 70 per cent of the spleens, and would seem to indicate that the number of malpighian corpuscles in a spleen remains constant until a fibrotic or some other pathological process becomes so marked that many of the corpuscles are completely destroyed or are made so small that they are not recognized.

Gross Pathology. As in the microscopical study, a consideration of the gross pathology consisted in the study of the 69 spleens of splenic anemia and a comparison with 175 specimens from the various other groups of splenomegaly.

The average weight of these spleens was approximately 950 gm., and the variations in weight 120 to 2290 gm. If patients less than ten years of age were excluded, the average weight increased to 1015 gm. Rolleston found the average weight in 21 cases of splenic anemia to be 782.46 gm.

When the average weight of these spleens was compared with that of the other groups of spleens of splenomegaly it was found that those of Gaucher's disease and those in the lymphoma group averaged higher in weight. The spleens arranged according to their number and average weights were: Gaucher's disease, four, 3031 gm.; the lymphoma group, five, 2249 gm.; splenic anemia, sixty-nine, 1015 gm.; pernicious anemia, fifty-three, 940 gm.; myelogenous leukemia, twenty-six, 937 gm.; hemolytic jaundice, thirty-two, 920 gm.; syphilis, six, 778 gm., and tuberculosis, four, 501 gm. It must be borne in mind that all of the spleens here considered were obtained at operation.

An effort was made to ascertain if the weight or size of the spleens varied in any other pathological conditions. Curves were made in order that any slight variation might be detected. When compared with the weight and size, there was no constant change found in the thickness of the capsule in the reticulum, in arteriosclerosis, or in the pulp or endothelium of the sinuses. The heavier spleens showed a slight tendency to have thicker capsules or a greater degree of perisplenitis. The spleen of splenic anemia maintained to a rather remarkable degree the shape of a normal spleen. From the standpoint of perisplenitis, the average was found to be +2. Thirty-eight were +2, eighteen +1, nine +3, and four +4.

Only 5 spleens showed macroscopical infarcts and these were variable in size, the largest being 12 x 8 x 3 cm. and the smallest scarcely perceptible. In these 5 specimens the average arteriosclerosis was +1.2. In 3 cases there was a history of abdominal pain and in 3 of gastric hemorrhage. In 3 cases also, ascites was present. All the changes mentioned, arteriosclerosis, pain, hemorrhage, and ascites were present in 1 case only. There was no constant clinical or pathological finding in the spleen in any of the cases of infarct.

A typical spleen of splenic anemia bears the general shape of a normal spleen, but is about five times as large. When allowed to rest on the table it maintains its shape much better than the normal spleen which flattens out; it is several times as firm as the normal. Its capsule is grayish-white with a slight reddish or a purplish-red tint. Hyaline plaques may or may not be seen on its surface; in the average spleen they would not be present. Perisplenitis is very evident, especially on the diaphragmatic surface.

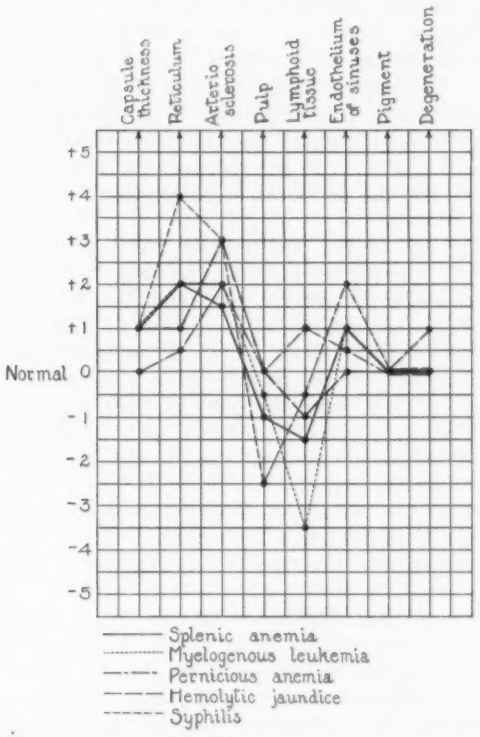

FIG. 5.—Microscopical pathological findings in splenic anemia, myelogenous leukemia, pernicious anemia, hemolytic jaundice and syphilis.

The typical spleen of splenic anemia offers considerable resistance to cutting. The cut surfaces bulge outward and present a red, beefy appearance. Fibrosis is very evident, and the trabeculæ are especially prominent. The malpighian bodies are not seen. The cut surface of a specimen that has been preserved in formalin is quite pink and the trabeculæ, which have become very white, form a prominent network over the surface.

When the results of the pathological study of splenic anemia are summarized and the findings are compared with a similar study of the other groups of splenomegaly, such as pernicious anemia, leukemia, and hemolytic jaundice, the general impression obtained is that there is a very great pathological variation within each group and that while certain conditions seem to be more common in some groups than in others, the findings overlap, to a great extent. The points of similarity in the various groups are rather striking and suggest that the spleen may play a similar part in all of the diseases that produce splenomegaly (Fig. 5).

Clinical Findings. The 69 patients with splenic anemia had been in poor health for an average period of seven years when they came to the Mayo Clinic. Because of the insidious onset of splenic anemia and the unreliability of the patient's memory, the possibility of inaccuracy in this statement is, of course, very great. Moreover, seven years does not indicate the entire duration of the disease, but the period of illness previous to the time of splenectomy.

The average age of the patients was thirty-three years, the youngest being two and one-half and the oldest sixty-nine years. If the average age is thirty-three years and the average duration seven years, the onset must have been about the age of twenty-six. The duration of the illness was in all probability more than seven years, for many of the patients gave a history of "always being delicate." They dated the onset of their illness, however, from the time of some marked disturbance, such as a gastric hemorrhage. The distribution was about equal in the sexes, there being 36 male and 33 female patients.

In no instance was a history of injury obtained as a possible cause, nor did the records show an instance of two or more cases of anemia occurring in the same family. Occupation was apparently not a factor.

Most of the patients complained of more than one abnormal condition which they considered of great importance in their illness. The complaints may be summarized as follows: Enlarged spleen and mass in left abdomen, 29; hemorrhages from the stomach, 20; and weakness, 19. Indigestion, pain in the left side of the abdomen and anemia were each complained of in 6 cases. Diarrhea was mentioned in 3, pallor in 3, pain in epigastrium in 2, shortness of breath in 2, and jaundice in 2; while rheumatism, constipation, palpitation, headaches, bleeding from the bowels, pain and numbness in legs, nervousness, and asthma were each mentioned but once.

The frequency with which hemorrhage occurred was rather surprising. It was not only a very common complaint, but often the severity of it was so alarming that it was a common cause for seeking medical attention. The histories showed that 41 of the

69 patients had hemorrhages. Thirty-eight of these were recognized by the patients as having come from the stomach as they had vomited blood, and 27, besides the vomiting of blood, had recognized blood passed by the bowel. Of the 3 remaining patients 1 noticed blood in the bowel movements only and 2 had quite profuse nasal bleeding. From the standpoint of severity, these hemorrhages may be graded 1, 2, 3, and 4. In 5 patients bleeding was graded 1, in eighteen, 2; in seventeen, 3; and in one, 4. Many of the patients spoke of the alarming nature of the hemorrhages; their prostration was so great that they had to remain in bed from three days to two weeks.

Abdominal pain was rarely mentioned as the chief complaint, probably its relative infrequency caused the patient to consider it of minor importance in his trouble. Nevertheless, on being questioned, 32 patients told of having had one or more attacks of pain, most of which were short, but often rather severe. Four of these patients located the pain definitely over the spleen; 2 had mid-epigastric pain, while 1 located the painful area in the lower right quadrant. There were 25, therefore, who were indefinite with regard to the site of the pain. According to Giffin, "Pain in the region of the spleen in splenic anemia is common and is probably due to perisplenitis which is so often present." Certain patients who complained of pain in the left abdominal area while under observation, presented definite friction rubs over the spleen.

Evidence was found elsewhere than in the spleen that might explain the pain in 15 of the 32 patients who had had pain. Six of those who complained of abdominal pain and one of mid-epigastric pain had gall stones; 4 with abdominal pain had diseased gall-bladders and 4 had chronic appendicitis.

Eight patients gave histories of having had malaria. None of these had had recent attacks nor had the disease lasted long. In all of them a special search had been made in the blood smears for the malarial plasmodia with negative results. Some investigators have taken exception to Banti's cases because they came from malarial districts. Geographical distribution of the patients in this series was: Minnesota 14, Iowa 8, Wisconsin 6, South Dakota 6, Illinois 5, Canada 5, Montana, North Dakota, Nebraska, Michigan, Missouri, and Texas each 2, and 1 each from Oregon, Indiana, Wyoming, New Mexico, New York, Pennsylvania, West Virginia, Kentucky, Tennessee, Mississippi, Alabama, and Arkansas.

Usually the first note made by the clinician in his physical examination was the size of the spleen. There was only 1 patient whose spleen could not be palpated and this might be explained by the presence of ascites; the spleen in this case weighed 390 gm. In 2 patients whose spleens could just be felt below the costal margin, the organs weighed 250 gm. and 425 gm. Another spleen, felt rather indistinctly and described as "a mass in the splenic region,"

weighed 318 gm. A spleen of 530 gm. was designated as "1 inch below the costal margin." On nearly every history chart a drawing was made by the examiner to show what he considered the relative size of the spleen. The size thus roughly designated varied in a general way with the weight in all except two instances. In these exceptions a spleen of 120 gm. and one of 320 gm. were outlined to suggest a much greater size. Judging from the diagrams on these histories a spleen that extended to the middle line and down to about the level of the umbilicus should weigh approximately 1000 gm. It would seem that the spleen maintained its relative position in the abdomen in spite of the enlarging process.

The adhesions around the spleen were so marked that special mention was made of them in 33 cases. There were, however, few spleens with elongated pedicles. On only one surgical card was reference made to the presence of a twisted pedicle. The spleen in 1 patient who had never had hemorrhages showed one complete turn; the organ weighed 610 gm.

In the physical examination the feel of the spleen was generally described by the clinician as "hard and smooth." A notch was felt in approximately 50 per cent.

Notes in the physical examinations regarding the size of the liver, referred to 24 as enlarged. Some of these organs, however, were apparently just below the costal margin and were marked "questionable enlargement." According to the operative findings, there were 26 patients who had enlarged livers. At operation 30 patients were found to have definite cirrhosis of the liver and in only 13 of these, was the liver larger than normal. The average weight of the spleen in the 24 cases in which the liver was described as enlarged was found to be 1016 gm.

Presumably, the size of the liver in splenic anemia bears no close relationship to the size and weight of the spleen. The findings in this series of cases suggest that there is a steady progressive enlargement of the spleen, but that the liver maintains its normal size until relatively late in the course of the disease. It then enlarges and may remain enlarged, or it may return to its normal size or become even smaller than normal. It cannot be said just how early in the disease cirrhosis of the liver begins. In many respects, therefore, the physical findings in splenic anemia are the reverse of those in portal cirrhosis, for in this latter disease a palpable spleen is usually found relatively late.

Ascites was present in 24 patients, 23 of whom had cirrhosis of the liver. In the other case the liver was enlarged, but apparently not cirrhotic. Allbutt and Rolleston are of the opinion that in splenic anemia ascites may occur in the absence of hepatic cirrhosis.

Only very general statements can be made with regard to weight lost during the progress of the disease. In most cases the disease

had lasted so long that the patient was uncertain as to his weight before onset. It would seem, however, that in a series of 22 cases, the average loss of weight was only 5 pounds. The greatest loss was 27 pounds, and 3 patients weighed more than what they considered their normal.

Bronzing of the skin is often mentioned in splenic anemia. In this series 21 patients were described as sallow or pale; 12 showed yellowness of the skin; 7 were described as lemon-yellow, 5 brownish-yellow, 1 tanned skin, 1 cachectic looking, and 1 brownish pigment about the eyes; 27, then, showed some change in the color of the skin; 21 of the remaining 42 patients showed sufficient pallor to attract attention. None of the patients appeared to have definite icterus.

In none of the histories was there a note concerning any enlargement of peripheral veins of the abdomen or chest.

From the standpoint of the laboratory work the blood count was undoubtedly the most valuable, but the reports on the coagulation time, fragility test, Wassermann reaction, and stool tests were not without value. Blood counts were made on all patients with splenic anemia before splenectomy, and on most of them at varying times after the operation.

The Wassermann test was done in 60 instances and was negative in 59. The 1 positive reaction was later discredited as a result of four subsequent negative tests. Four patients gave a history of syphilitic infection, but in none of these could evidence of syphilis be found.

Stool examinations were seldom done. There were apparently two indications; a history of diarrheal attacks, or of residence in the tropics. Thirteen stool examinations were done with the following results: 9 were negative; 2 showed *Amœba histolytica;* 1 *Lamblia intestinalis*, and 1 cercomonads and trichomonas. None of the patients, however, had diarrheal attacks.

The fragility test was done in 29 of the patients. In 15 of these the fragility was normal; only 1 showed a tendency toward an increase in fragility of the corpuscles, while 13 showed an increased resistance.

The coagulation time was determined in only 13 patients. All except 1 were between two and ten minutes. One patient showed a coagulation time of fifteen minutes. In this determination either the Biffi-Brooks coagulometer, the Boggs coagulometer or the Lee and Vincent test-tube method was employed.

A study of the relation between the number of erythrocytes and leukocytes and the hemoglobin before operation revealed a varying degree of anemia. In every case this was of the secondary type, the color index in many cases being relatively low. There was always a relative leucopenia and in some of the counts the number of leukocytes was low in comparison to the number of red corpuscles.

The average erythrocyte count was 3,700,000, the hemoglobin 53 per cent, and the leukocytes 4900. In the 30 patients with definite cirrhosis of the liver, the erythrocytes were about 3,500,000, the hemoglobin 50 per cent and the leukocytes 4600. In the 13 patients with enlargement of the liver but without definite cirrhosis, the erythrocytes were about 4,000,000, the hemoglobin 56 per cent, and the leukocytes 5800. The remaining 26 patients who had approximately normal livers had an average erythrocyte count of 3,750,000, hemoglobin of 55 per cent, and a leukocyte count of 5000.

In many of the patients, changes in the erythrocytes were noted and were usually designated as slight or moderate. These changes were seen in patients with the greatest degree of anemia. Poikilocytosis and anisocystosis were noted in 29 of the 69 patients; anisocytosis, poikilocytosis and normoblasts in 12; and anisocytosis alone in 9. Only occasionally, mention was made of polychromatophilia.

In most of the patients blood counts were made at varying intervals after splenectomy and in every case there was a marked increase in the number of leukocytes. The normal was taken as 8000, and in each case the number of days after operation was considered. A composite chart showed that there was an initial rise in the leukocytes immediately after the operation and that the number gradually increased until about the forty-fifth day. There was then a gradual decrease until the count approached the normal line in seventy-five to one hundred days after splenectomy. An abrupt rise occurred previous to the tenth day after splenectomy. From the tenth to the thirtieth day the increase was more gradual. A very gradual decrease then followed until the normal line was approached.

An attempt was made to determine how long secondary anemia persisted after splenectomy, but the results were rather inconclusive. It is certain, however, that there was an improvement in the hemoglobin and the number of erythrocytes. The degree of improvement varied greatly so that no time relation could be established. In only a very few cases were two or more blood counts made following splenectomy and, while these showed progressive improvement, the number was too small from which to draw conclusions.

A differential cell count was made in 63 of the patients before operation. In the remaining histories the count was noted as normal, and so had to be discarded. If the normal number of polynuclears be considered as varying between 60 and 70 per cent (Piersol), the preoperative counts in these cases were normal in 24 cases, below normal in 10, and there was a relative increase in 29. According to Pappenheim the number of lymphocytes found in a normal differential count is from 20 to 22 per cent. When

the lymphocyte counts were compared with these standard figures it was found that 10 were within the limits of normal, 30 above normal, and 25 below normal. A comparison was next made between the preoperative and postoperative differential counts. In 35 patients one of the differential counts had been omitted. Postoperatively 10 patients showed an increase in the polynuclears, and 22 showed an increase in the relative number of lymphocytes. Two patients showed practically no changes in the blood following operation. The length of time that elapsed after splenectomy seemed not to have been an important factor. In patients with an increase in the polynuclear cells, however, the differential count had been made from seven to forty-three days after operation.

Most of the operative findings have already been discussed, but the condition of the gall-bladder as found at operation only has been considered in part. In 11 cases it was described as diseased, markedly distended, or as having a thick wall. In 8 patients the gall-bladder contained stones.

The vermiform appendix was diseased in 7 patients and the extent of disease +2 or +3.

Patients with Cirrhosis of the Liver. There is considerable confusion in the literature with regard to the relation between Banti's disease and splenic anemia. Most American writers choose to consider the two as entirely synonymous, while foreign authors prefer to make a well marked distinction between them.

MacCarty, of the Mayo Clinic, has examined specimens of hepatic tissue obtained at operation is nearly all of the 69 cases of splenic anemia here reported and he is of the opinion that in none of them, no matter how short the duration of the disease, was the liver entirely normal. From the mildest case to the most severe, the liver showed varying degrees of hepatitis. In the more severe types, periportal fibrosis was evident, but there was no sharp line of distinction between those with well defined cirrhosis and those without.

Thirty cases in which there was definite evidence of portal cirrhosis have been grouped together. From the standpoint of morbid anatomy these 30 spleens very closely resembled the remaining 39. Their average weight was a little greater, being 1027 gm. as compared to 1015 gm. of the entire series. There was a slight increase in the amount of fibrosis, but in all other respects no difference could be made out.

This close similarity was found also in the microscopical study. Each pathological finding was graded and averaged as in all the other cases and the results were expressed in a curve. This curve was found to correspond exactly with that for splenic anemia; except that the splenic pulp was −1.4 instead of −1.

The clinical study of this group showed interesting variations from the entire series of cases. The average age was thirty-five;

duration of disease was nine years. As in the other cases, most of the patients dated the origin of the disease, not from the time of the real onset, but probably from the time of some severe manifestation, such as gastric hemorrhage. Nineteen of these patients gave a history of hemorrhage, the severity of which was no greater than that of the remaining 22 patients who also complained of hemorrhages. Eighteen had gastric hemorrhages; 14 had also noticed blood passed by the bowels, and 1 had nasal bleeding; 1 complained of melena only.

In the chief complaints hemorrhages were mentioned 11 times, while enlarged spleen and abdominal mass, if considered together, were complained of 12 times. The less important complaints in order of frequency, were stomach trouble, 5; anemia, 4; abdominal pain, 4; weakness, 4; jaundice, 2; dyspnea, 1; constipation, 1 and pain in the legs, 1.

While most writers consider true Banti's disease to include all patients with definite cirrhosis of the liver, according to Banti there should be ascites besides the cirrhosis. Ascites was rather common in this group, being noted in 24 patients who could, therefore, be classified as cases of true Banti's disease. In 10 of these it was sufficiently marked to be noticed before operation. Thirteen of the 30 patients had enlargement of the liver. An effort was made to find some difference between the 24 cases which showed ascites and the remaining 6 cases of the cirrhosis group. Practically no difference could be made out and for this reason a separate discussion of the group of true Banti's disease would be but a repetition of that given on the group of patients with decided cirrhosis of the liver.

A comparison of the postoperative mortality in patients with cirrhotic livers with that of the remaining patients was interesting. In the 69 patients the highest mortality occurred within forty days of the operation; 12 had died within this period, and 7 of these were patients with marked cirrhosis. If these figures are expressed in terms of percentage, it is seen that 23.3 per cent of the patients in the group with cirrhosis died within forty days of the operation, while only 12.8 per cent of the other patients died within the same length of time.

In splenic anemia the condition seems to be one of under function of the spleen rather than of over function. In the conflict with disease, while all the body tissues suffer, the spleen seems to bear the brunt of the battle. As the normal tissue of the spleen is destroyed it is replaced by fibrous tissues and the organ enlarges in an attempt to keep up its struggle against the disease. Finally, the spleen decompensates and, instead of being a help, it becomes a menace and may be a focus from which the disease is better able to attack the liver and the other organs.

This suggests the question of the most advisable time to perform

splenectomy in cases of splenic anemia. From the standpoint of the operative mortality alone the spleen should certainly be removed before definite hepatic cirrhosis has occurred. In the future the development of some test of hepatic function may indirectly be an index to the functional activity of the spleen.

The Mortality and the Postmortem Reports. A general summary of the deaths in this series of patients with splenic anemia has been given by Giffin. There were 9 deaths in hospital and 6 of these patients showed a definite cirrhosis of the liver. It would seem, therefore, that cirrhosis of the liver, especially if associated with ascites, is a very great factor in increasing the operative risk in this disease.

Summary. 1. A composite picture of the pathological findings in the spleen in splenic anemia was found to be one of generalized fibrosis. There were no findings in the splenic tissue that would enable the pathologist to make a positive diagnosis of splenic anemia, yet the abnormality was as characteristic of this disease as in other diseases producing splenomegaly.

2. The degree of fibrosis of the reticulum seemed to vary in a slight degree with the amount of arteriosclerosis. There was no evidence to show, however, that this fibrosis originated in or around the vessel walls.

3. The size of the malpighian corpuscle seemed to be affected by the degree of fibrosis and the greater the fibrosis the more eccentric was the so-called central artery.

4. The splenic veins presented no marked abnormality or evidence of thrombophlebitis.

5. Dilatation of the sinuses was fairly constant and the reticular cells showed a proliferative activity. The syphilitic spleens resembled those of splenic anemia in this respect.

6. The amount of lymphoid tissue present was usually below normal. The malpighian corpuscles were fairly well defined, but the so-called germinal centers were small and seldom seen. Areas of degeneration or fibrous nodules were not found in the malpighian bodies.

7. As a result of an actual measurement it was found that the size of the malpighian corpuscles was within the limits of normal, but that the average size was below the average for the normal. The number of corpuscles for each square centimeter was found to be twenty-three.

8. By actual figures 70 per cent of the spleens showed that the number of malpighian bodies for each square area decreased and the size of the corpuscles became smaller as the size and the weight of the spleen increased.

9. The average weight of the spleens was found to be 1015 gm.

10. The average age of the patients with splenic anemia was

thirty-three years, and the number of males was about equal to the number of females. There was apparently no familial tendency.

11. The most common complaints were mass in the left abdomen, gastric hemorrhage, and weakness.

12. While abdominal pain was rarely given as the chief complaint, the histories brought out the fact that 32 of the patients had attacks at some stage of the disease. In many instances the pain was probably due to perisplenitis.

13. In the physical examination spleens designated as just palpable weighed from 250 to 500 gm., while spleens of approximately 1000 gm. extended to the middle line and almost to the level of the umbilicus.

14. The relation of the size of the spleen, as given by the clinical records, to the actual weight, and the fact that many adhesions were found at operation, suggested that the spleen of splenic anemia maintains its relatively normal position in the abdomen.

15. Physical examination showed 24 enlarged livers, while at the operating table 26 showed a definite cirrhosis, and 13 were larger than normal. The size of the liver seemed to have no relation to the size and weight of the spleen.

16. In the 69 patients the average erythrocyte count was 3,700,000, the hemoglobin 53 per cent, and the leukocyte count, 4990. The coagulation time and the fragility test were normal, and the Wassermann tests and the stool examinations were negative.

17. A composite chart of the blood counts made after the operations showed a gradual increase in the leukocytes up to the forty-fifth day. There was then a gradual decrease until the normal was reached in about seventy-five days. A similar result was obtained in a composite chart in which the number of leukocytes found in the counts made before the operation was taken into consideration.

18. A comparison of the number of lymphocytes in the differential count showed that the average was within the limits of normal. A lymphocytosis did not seem to be a characteristic in this series.

19. In the study of the liver tissue in the cases of splenic anemia, 30 showed a definite cirrhosis, but in none was the liver entirely normal.

20. The chief complaints of the 30 patients that had hepatic cirrhosis were the same as those in the rest of the series; hemorrhage and abdominal mass were the predominating complaints.

21. Twenty-four of the patients with cirrhosis of the liver had ascites.

22. Twenty-three and three-tenths per cent of the patients with cirrhotic livers died within forty days of the operation, while within the same length of time the death rate of the remaining patients was only 12.8 per cent.

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ELEPHANTIASIS: A CLINICAL REVIEW AND AN ATTEMPT AT EXPERIMENTAL REPRODUCTION.*

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Various definitions of elephantiasis have been given. Practically all refer to the hypertrophy of the skin and subcutaneous connective tissue with vascular disturbances and resulting exudate. The congenital form of elephantiasis usually involves one or more limbs. The pathological picture differs from the true form in that connective tissue hypertrophy and normal cell infiltration are absent.

No one has been able to obtain cultures of bacteria except during the recurring active cutaneous reactions seen in the majority of cases of elephantiasis. It must be remembered, however, that a few cases of elephantiasis occur without local inflammatory manifestations. Sistrunk had several of this type in his series. Bac-

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teriological studies were made in most of the cases. In one of these in which there had never been local inflammation, Magath was able to grow, in pure culture, a green-producing streptococcus. In another case in which there were local manifestations he was able to isolate practically the same organism from the deep tissues during a period of quiescence.

Etiological Factors. Manson has traced the life cycle of the filaria which he considered the etiological factor. Objections have been made because central blockage of the lymphatics cannot produce peripheral edema, and because it has been impossible to find filaria in the blood of patients with well developed elephantiasis, who, at some former time, were known to have been hosts of the filaria. Manson did not attempt to explain the former criticism, but the second issue was well known to him. He believed that the lymph blockage was accomplished by the death of the parent worm, which was caused by the lymphangitis observed in all cases of elephantiasis that he studied. He also believed that trauma to the part harboring the parasite would cause the premature parturition of the ova which, being larger than the embryo filaria and not having power of motion, would cause blockage of the lymphatics.

Blockage of the lymphatics with subsequent edema is not sufficient to explain the connective tissue hypertrophy which is the most characteristic histo-pathological element of the disease. An abundance of experimental proof as well as an enormous amount of clinical material indicate that edema will not excite cell proliferation.

Distribution: Age and Sex. Elephantiasis has not been recognized as a transmissible disease, although a few reported cases would indicate that it might be. Tuberculosis and syphilis have a questionable relationship to elephantiasis. Operative interference with the inguinal lymphatics has preceded some cases of genital elephantiasis. A preponderance of data favor the idea that the edema and hypertrophy which characterize elephantiasis develop as the result of the action of pathogenic organisms, even though it has not been proved that a specific organism is responsible for the disease. It is the exceptional case that did not begin following lymphangitis, cellulitis, dermatitis, or some manifestation of a local infection. In a few cases onset has been insidious, without symptoms, either local or general, that would lead one to think of an infectious process. This has been observed many times. Webb mentions the same type of case observed by him in India.

Elephantiasis is observed in all parts of the world; but as an epidemic it exists only in certain circumscribed areas in the tropical or subtropical regions. In the United States and Canada, it is uncommon and never epidemic.

In the 33 cases studied in the Mayo Clinic the youngest patient was aged twelve, the oldest fifty-five years. In tropical countries,

men are affected more often than women, supposedly on account of injuries and infections to which they are more often subjected. Women and men were affected about equally in the cases reported from the Clinic.

Pathological Findings. Most authors have represented the same pathological findings in elephantiasis. Paget describes elephantiasic tissue as "closely woven and very tough, and on section to exude a whitish fluid." Pusey considers hypertrophy of the subcutaneous tissue the most characteristic feature; he said that the hypertrophy converts the part into a dense fibrous structure in which are usually found dilated lymph spaces. The chorium is greatly thickened, and the matting together of its layers disorganizes its typical arrangement. The epidermis may or may not be thickened. The sebaceous glands, sweat glands, and hair follicles may be unchanged or destroyed. Stelwagon agrees with Pusey that the chief change is hypertrophy of the connective tissue, but he contends that the blood-vessels are also changed, and adds that Mosely and Morrison found an increase in the pigment matter. Hartzell draws attention to a plugging of the veins with a thrombus composed of leukocytes. Elliott believes that there are more changes in the arteries than in the veins. Unna believes that the condition begins quite superficially by a blocking of the veins from the inflammatory process excited by the bacteria. There is a subsequent destruction of some of the vessels, with still more edema, and the ever present bacteria, lying latent in the tissue ready to flare up, produce still more hypertrophy of the tissue, thereby interfering more with the circulation. This chain of events continues until finally there is an enormous tissue hypertrophy, with destruction of many superficial blood-vessels draining the part, and resulting edema.

In the cases of elephantiasis studied, the epidermis was thinned out when the extremity was unusually large. There was always some change in the blood-vessels. Occasionally there was a marked thrombosis and lymphocytic infiltration around the vessel, especially in patients who had had violent cutaneous reactions. The lymphocytic infiltration was always mild in the patient who had not suffered from recurring attacks of erythema; but some of the sections representing the most marked hypertrophy were obtained from patients who had never had erysipelas, cellulitis, or any symptom to indicate inflammation in the part. In such cases there was more evidence of lymphocytic infiltration in the deeper layers, and the aponeurosis was often more thickened; also, there were more changes in the bloodvessels of the deeper tissues than in the chorium. It may be assumed that in many patients who develop elephantiasis, the inflammatory reaction necessary to produce cell proliferation is caused by low-grade organisms confined to the subcutaneous tissue and not of sufficient virulence to produce local or constitutional reactions.

SURGICAL TREATMENT. Mann calls attention to the two principles which, at present, are the basis for the surgical treatment of this condition: (1) establishing new lymph paths; and (2) connecting the edematous elephantiasic tissues with the normal musculature below the aponeurosis.

Sistrunk has performed a modified Kondoleon operation on about 40 patients with elephantiasis. He removes, besides the aponeurosis, a wide piece of skin and subcutaneous tissue nearly, though not quite, so wide as the aponeurosis. Recently he has also removed small sections of the aponeurosis in the iliac regions in patients with the disease especially pronounced in the thighs and hips. Sistrunk believes the removal of large pieces of diseased skin and subcutaneous tissue (not capable of functioning because of the destroyed vascular lymph supply) is of great importance.

If these patients are kept in bed for a week or more before operation, the parts will be reduced in size and operation made easier. Morphine given before operation minimizes the shock. In extreme cases, a complete operation cannot be performed at one time, but similar operations on different portions of the extremity may be performed at different times. Operation does not cure elephantiasis, but the condition can be greatly relieved. Better results will be obtained if the patients wear elastic stockings indefinitely, perhaps permanently.

Experiments. Since I believed that the hypertrophy and edema which characterize elephantiasis is caused directly by the action of pathogenic bacteria, I attempted to prove it by experiments on dogs. Bockhardt injected a culture of living organisms (the coccus of Fehleisen) into the tissues of a pedunculated malignant tumor which subsequently took on changes typical of elephantiasis. In a series of experiments on animals, an attempt was made to lower the resistance of the part by interfering with the lymphatics draining the region. Later, the venous return was also partially ligated, further to lower the resistance of the part. The animals were then inoculated with a green-producing streptococcus obtained by Dr. Magath from the subcutaneous tissues of two patients in Dr. Sistrunk's series. Dr. Magath describes the technic used and the type of organism cultured as follows:

"A small piece of tissue taken from the leg (elephantiasis) was introduced directly and immediately into a tube of glucose broth, and incubated for forty-eight hours. At the end of that time a smear made from the broth showed numerous small, short chains of streptococci. Transfers were made by streaking a plate of blood agar; the streptococcus was present in pure culture. The colonies were minute, semi-flattened and circular, growing slowly with the formation of a slight amount of green pigment, less than *Streptococcus viridans* but more than typical pneumococcus. The broth culture was used for the first animal injection, and sub-

cultures taken from this in broth were used for subsequent injections. A similar organism was isolated from a piece of tissue taken from the scrotum of another patient with elephantiasis, and this was used for the last series of animal inoculations."

Twenty animals were used. To favor the development of the organism, the lymphatics of the groin of the leg were dissected out. In others, the femoral vein was also ligated. Controls were used. The injections of the organisms were made intravenously and subcutaneously in different groups of the animals. The intravenous injections were made on the evidence that a blood-borne organism is responsible for the condition. The opposite leg from the one in which the lymphatics or veins, or both, were molested, was used for the injection. We undertook this work with the full understanding that the production of a chronic lesion in an animal offered many difficulties. It is well known that animals may not respond to certain organisms as does man. Moreover, the cultures used must be kept under artificial conditions for a long time and would lose some of their activity.

In some of the experiments neither the operative procedure nor the injected bacteria produced any noticeable effect. In many instances the removal of the lymphatics, and particularly the ligation of the venous return, produced edema of the leg for a variable period. The edema did not persist for any great length of time and a condition resembling elephantiasis never occurred. The effect attributable to the bacteria was obtained. The results of the experiments were negative with regard to the production of elephantiasis.

Conclusions. 1. The characteristic feature of elephantiasis is a hypertrophy of the collagenous connective tissue with some degree of lymph and venous stasis.

2. The hypertrophy of the connective tissue and the corresponding stasis are probably the result of repeated insults from pathogenic bacteria.

3. In one group of cases of elephantiasis, there is an outward manifestation of infection evidenced by erythema and adenitis. This type is more common. There is a second group in which the disease develops insidiously, and without any local manifestation of infection. From the pathological study of these cases, I am convinced that they too have an infection basis, which is confined to the lower layers of the subcutaneous tissue, and of such low grade as not to excite any local symptoms.

4. Anything that causes venous stasis could be considered a predisposing factor in the development of elephantiasis.

5. Central blockage of the lymphatics probably cannot produce permanent peripheral lymph stasis.

6. The parent worm of filaria may excite inflammatory changes, and elephantiasis may be produced in such cases by pathogenic bacteria, the filaria being a predisposing factor.

7. In the Kondoleon operation, we have a means of rendering useful service to patients with elephantiasis, although the operation does not positively cure the disease.

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A STUDY OF URINARY OUTPUT AND BLOOD-PRESSURE CHANGES RESULTING IN EXPERIMENTAL ASCITES.*

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In the following paper it is intended to present some simple experimental data dealing with artificially increased intra-abdominal pressure, in the attempt to elucidate the mechanism of some common vascular and renal secretory changes which occur in association with ascites.

* The writers desire to express their thanks to Prof. A. N. Richards for laboratory facilities and valuable suggestions, and to Dr. A. B. Light for technical assistance in connection with these experiments.

The physician who carefully studies patients whose condition is complicated by ascites (the usual case is cardio-renal), will notice that this is accompanied by a diminution of urinary output and that paracentesis abdominalis for removal of a fluid collection is usually accompanied by a slight rise of blood-pressure. The urinary output is in a measure restored to normal by the operation of paracentesis.

These features are not satisfactorily explained, either in textbooks on physiology or physical diagnosis. Nowhere does one discover any mention of the influence of ascitic effusions upon either caval circulation or renal output. Krehl[1] makes the following statement, which is quoted as bearing on the problem under consideration: "If the quantity of blood that flows through the kidney be diminished, a small amount of highly concentrated urine is secreted; in other words, the diminution in the total solids is not parallel to that of water. . . , a diminished renal circulation may occur in the absence of any local constriction of the renal vessels, either because the general arterial pressure is reduced or because the pressure in the renal veins is raised. The reduction of the general arterial pressure may result from a wide-spread vasomotor paralysis or from a weakening of the left ventricle. The pressure in the renal veins may be raised by an occlusion of these veins, or of the vena cava inferior; by an increase in the general venous pressure from a weakening of the right ventricle; or by a diminution in the aspirating action of the thorax."

It has been shown by Paneth,[2] and later by de Souza,[3] that every venous obstruction in the kidney lessens the urinary output as soon as it reaches a certain (moderate) degree.

That the presence of fluid in the abdomen causes a diminution of urinary output in cases in which but little renal pathology is demonstrable, is illustrated by the following history.

CASE REPORT. Mary S., aged fifty-three years. Admitted March 27, 1921.

Chief Complaint. Decreasing urinary output. Abdominal swelling.

Present Illness. Patient was well until four weeks ago, when abdominal soreness and swelling began. Urinary output has steadily decreased. No dysuria; never any hematuria. Ankles have not been swollen. No dyspnea nor palpitation. Sleeps poorly. Appetite good. Constipated.

Past Medical History. Always well except for dyspepsia.

Family History. Husband living and well. Seven children living and well.

Social History. Housework. Born in Ireland; in United States thirty years. Drinks tea and coffee, alcohol in moderation.

Physical Examination. Well developed adult white female. The examination of the head, neck, chest and extremities was negative.

Abdomen: Liver and spleen not enlarged. Abdomen much distended and resistance is encountered although no mass is palpable. Dulness in the flanks with coronal tympany. No areas of tenderness.

Gynecological Examination. Bilateral and perineal lacerations. Uterus not enlarged; fixed but not tender.

Diagnosis. Rapidly growing mass; origin undetermined. Advice: Laparotomy.

Clinical Notes. March 28. Has voided only 2 ounces since admission. One ounce of urine obtained on catheterization. Patient feels all right except for abdominal distension.

March 29. Roentgen-ray report: Irregular shadow in lower abdomen, probably due to large mass.

Cystoscopic report: Bladder depressed anteriorly and trigone markedly elevated. Both ureters catheterized for 27 cm. without encountering any resistance. Passage of catheters not followed by any material quantity of urine sufficient to indicate hydroureter or hydronephrosis. Indigo-carmine, right, nine and a half; left, eleven and a half minutes after injection.

Operation. Abdomen opened below umbilicus. Peritoneum thickened and adherent. About 1.5 gallons of straw colored fluid poured out, apparently contained in two or three large cavities formed by intestinal adhesions. Mesentery and omentum were thickened and friable, while a chain of thickened and enlarged glands ran along the mesenteric attachment throughout the length of the small intestine. Diagnosis: Carcinoma; impossible to determine the primary focus. Kidneys on palpation appeared to be normal. Enlarged glands and a piece of thickened omentum were removed for section. Abdomen closed with drainage.

March 31. Patient much more comfortable. Urinary output has greatly increased.

Tissue Diagnosis: Scirrhous carcinoma.

The following are laboratory findings for the first twelve days following the patient's admission to the hospital:

Urine. The specific gravity varied between 1020 and 1030. A very faint trace of albumin was found on the first examination otherwise the results were negative. The volume output in twenty-four hours was between 210 to 270 cc before operation; after operation this was between 500 to 900 cc. The phenolsulphonephthalein was 15 per cent in two hours.

Blood. Wassermann, negative. Urea nitrogen, 19 mg. per 100 cc.

Blood-pressure. March 28, 130 to 65. April 5, 120 to 70.

Abdominal Fluid. Polymorphonuclears 33 per cent, lymphocytes 67 per cent. Negative for tubercle bacilli.

We have here an example of massive ascites, due to rapidly progressing malignancy, in which, with no apparent renal pathology, urine output is greatly cut down; with removal of the ascitic fluid, urinary output immediately returns to a volume approximating the normal.

The intra-abdominal tension required to produce a diminution of urinary output is not great. Two patients whose intra-abdominal tension was measured by means of trocar and attached mercury manometer, registered pressures of 15 to 20 mm. This agrees with the measurements of Quirin,[4] who records 20 mm. as the intra-abdominal pressure in two patients, each with an ascites amounting to about 7000 cc.

Experimental Studies. To obtain further information concerning the conditions which caused such marked changes in urine excretion in this patient, four experiments were performed in which intra-abdominal pressure of dogs was raised by injecting fluid into the peritoneal cavity, urinary output being measured at varying degrees of intra-abdominal pressure.

Procedure. Female dogs, of approximately equal size, were used; to minimize as far as possible suppression of urine due to anesthetic and operation, they were given glucose solution by stomach tube, about twelve hours and again two hours before the experiment began. Anesthesia was induced by intramuscular injection of luminal, as a rule, supplemented by ether inhalation. Carotid blood-pressure was recorded by a mercury manometer. Through a midline abdominal incision, a cannula was inserted into each ureter, and these were connected to a glass tube which passed through the urethra; urine excretion was measured either by volume or in drops. The rectum was divided and a glass tube introduced through the anus; this tube was connected to a pressure bottle containing the fluid to be introduced and to a vertical glass tube which acted as a manometer, the pressure readings being given in millimeters of mercury in the following sections. The abdomen was then closed tightly.

The fluid was kept at 37° to 40° C., and, when it was desired to raise intra-abdominal pressure, was forced into the abdomen by way of the rectum by pumping air into the pressure bottle containing the fluid. In three experiments, 0.9 per cent saline was used; in the fourth, 5 per cent acacia was added, in the hope of diminishing the absorption rate of the fluid. There were no apparent differences in the results obtained with the two solutions.

Results. Urine excretion was always totally suppressed when abdominal pressure was raised to 30 mm. of mercury. Pressures lower than 15 mm. had no constant effect on rate of urine flow,

but from 15 to 30 mm. there was always constant diminution. (Figs. 1, 2 and 3).

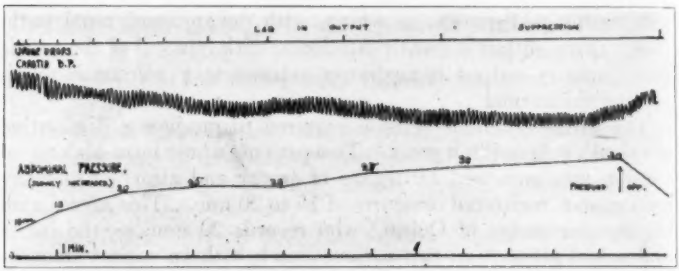

FIG. 1.—Tracing to show decrease in urinary output and suppression of urine which follows a gradually raised intra-abdominal pressure. A slight fall of carotid blood-pressure is also to be noted.

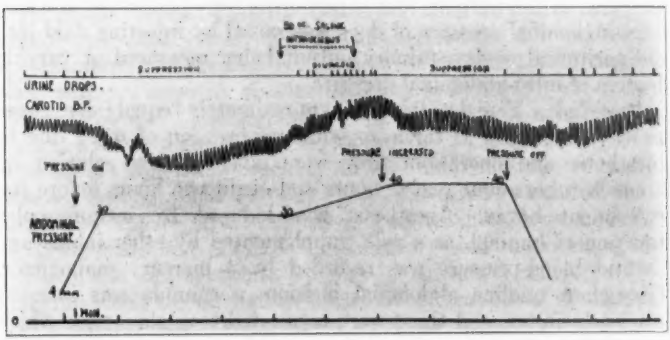

FIG. 2.—Tracing to show urinary suppression following increased intra-abdominal pressure, and the diuresis which may occur, at suppression pressure, when saline is introduced intravenously.

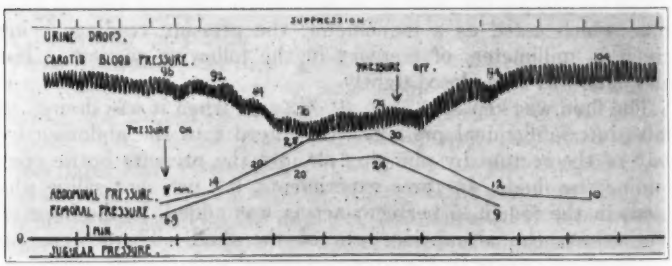

FIG. 3.—Tracing to show the effect of varying intra-abdominal pressure upon urine output, carotid blood-pressure, femoral pressure and jugular pressure.

On releasing abdominal pressure, by allowing fluid to flow back into the bottle, urine usually began to appear promptly; in one

experiment there was total suppression at 30 mm. abdominal pressure, while urine reappeared at an intra-abdominal pressure of 28 mm. (Experiment 2), demonstrating the constancy and abruptness of the suppression threshold (Fig. 1 and 2).

Accompanying a rise of intra-abdominal pressure from zero to 30 mm. there was usually a fall of 5 to 10 mm. in carotid blood-pressure (Figs. 1, 2 and 3).

These changes in urine secretion might have been due to pressure on the ureters, to changes in the general circulation, or to pressure on the renal veins.

That the suppression was not due to compression of the ureters, is shown by the results of injecting saline intravenously while urine flow was inhibited by an abdominal pressure of 30 mm. Such an injection was always followed by a profuse flow of urine, which could be readily inhibited by raising intra-abdominal pressure to 35 to 40 mm. (Fig. 2, Experiment 2.)

Changes in the general circulation were not constant, but usually there was a fall of 5 to 10 mm. in blood-pressure when intra-abdominal pressure was raised sufficiently to suppress urine. This fall is scarcely enough to cause total suppression of urine, and urine was often excreted readily at a considerably lower level of blood-pressure, if abdominal pressure was low. Furthermore, blood-pressure might fall less than 5 to 10 mm., and in one instance it rose as abdominal pressure was raised (Experiment 2); often, after a primary fall, blood-pressure rose while intra-abdominal pressure was held at 30 mm. until it was higher than before the fluid was injected into the abdomen, but no urine appeared. In every case, urine was suppressed by an abdominal pressure of 30 mm. regardless of the blood-pressure level.

Of all the structures concerned in the normal renal function, the renal veins are most susceptible to external pressure, since pressure within the inferior cava is normally only a few millimeters of mercury. Consequently, onward flow in this vessel must cease when pressure upon it becomes greater than pressure within it, and could only be maintained by a rise in venous pressure to a point equal to the external pressure.

To determine the presence of a rise in venous pressure, vertical glass tubes, coated with wax, were connected with a femoral and an external jugular vein, while abdominal pressure was raised and lowered. Blood rose in the femoral tube to a height almost exactly equivalent to existing abdominal pressure, and rose or fell proportionately as abdominal pressure was raised or lowered. There was no appearance of blood at any time in the jugular tube, though saline flowed readily and completely from the tube into the vein (Fig. 3, Experiment 2).

The rise in venous pressure must, therefore, have been due to factors operative only below the diaphragm.

In order to determine if this rise in venous pressure was effective at the point of entrance of the renal veins, a small catheter, coated within by means of solid sodium citrate, was connected to a vertical tube and its tip introduced into a femoral vein.

Blood rose in the tube to a height equivalent to the existing abdominal pressure. The catheter was pushed on within the inferior cava, with no change in height of the blood column, until the tip of the catheter reached a point just above the diaphragm, when all the blood flowed rapidly out of the tube (Experiment 3).

The catheter was then introduced into the left external jugular vein and pushed on until its tip was in the inferior cava. There was no rise of blood in the tube as long as the tip of the catheter was above the diaphragm, but as soon as it passed below, blood rose to a height almost equivalent to abdominal pressure.

A rise in intra-abdominal pressure is thus seen to cause a rise in abdominal venous pressure, and this is effective throughout the entire inferior caval system below the diaphragm. Its effect on renal function is directly comparable to the effect of partial occlusion of the renal veins, which uniformly causes partial or complete suppression of urine (Paneth; de Souza).

The first effect of a sudden increase in intra-abdominal pressure is probably a collapse of the inferior cava, for venous pressure is lower here than in its tributaries. Consequently, filling of the heart must be interfered with until venous pressure rises sufficiently to overcome the external pressure, and the fall in blood-pressure which follows a sudden, though comparatively slight increase in intra-abdominal pressure is probably due to this. The ultimate level maintained by blood-pressure when intra-abdominal pressure is held at a high level must depend, to some extent at least, on the proportion of total blood volume required to maintain the higher level of abdominal venous pressure, and which is thereby lost to the effective circulation.

Under such circumstances of increased intra-abdominal pressure, abdominal venous pressure must rise to a point almost, if not exactly, equal to the intra-abdominal pressure, and measurement of the latter is, therefore, an index of the pressure against which the renal circulation is working.

In experiments in which fluid was injected quite rapidly into the abdomen, 750 cc always raised the intra-abdominal pressure to the suppression point of urine (30 mm.) while 1000 cc caused marked respiratory distress.

When fluid was introduced gradually (Experiment 4), so that time was allowed for compensation to occur, 2100 cc was required to raise intra-abdominal pressure to 30 mm., and this relatively enormous volume caused no apparent distress. Beyond this point, however, slight increases in volume of fluid caused marked pressure symptoms, due, apparently, to yielding of the diaphragm,

and after 2400 cc had been introduced, blood-pressure fell sharply to zero, the heart giving a few spasmodic beats, but entire recovery occurred promptly when fluid was allowed to escape. It was now possible to reinject rapidly almost 2000 cc of fluid before any symptoms resulted, and at least 300 cc must have remained in the abdominal cavity.

Apparently the abdominal muscles lose their tonicity when gradually distended, and in this way large volumes of fluid can be accommodated in the abdominal cavity without the extreme rise in intra-abdominal pressure seen when much smaller amounts are rapidly injected. The diaphragm seems to retain its tone much longer, but, once it yields, a slight further increase in pressure causes prompt and very marked disturbances of the circulation, these being probably due to an occlusion of the great veins, so that filling of the heart is prevented. Pressure on the ventricles direct would probably not cause so sudden a failure.

Protocols. *Experiment* 1. To determine the effects on urine excretion and blood-pressure of sudden changes in intra-abdominal pressure.

Female fox terrier, 5.8 kilos, was given 400 cc of 5 per cent glucose, by stomach tube, at 9.30 A.M.; luminal, 0.12 gm. per kilo, at 10 A.M. Ether during operation only. Tracheal cannula; left carotid connected to manometer. 0.9 per cent saline was used to raise abdominal pressure. Urine output was measured in cubic centimeters per three minute period.

Time.	Blood-pressure.	Abdominal pressure.	Urine cc per 3 minutes.	Conditions.
4.00 4.12	78	0	0.30	Control.
4.15	72	30	0	750 cc saline injected into abdomen; suppression.
4.18	66	25	0.05	Fluid held in abdomen.
4.30	64	6	0.08	Fluid flowing back into bottle.
4.33	66	4	0.45	Recovery.
4.48	74	4	0.1	Recovery.
4.51	82	30	0	750 cc saline injected into abdomen; blood-pressure rises; suppression.
5.06	82	12	0.1	Fluid flowing back into bottle.
5.12	90	10	0.13	Recovery.
5.18	98	8	0.4	Recovery.

If the injection of fluid be performed more slowly, it causes a progressive lag in urinary output and complete suppression, when the intra-abdominal pressure reaches 30 mm. (Fig. 1).

Experiment 2. A. To determine whether compression of the renal pelvis or ureters by the intra-abdominal pressure is a factor in the suppression; to determine whether, at the intra-abdominal suppression pressure, diuresis may be produced by increasing arterial blood-pressure (Fig. 2).

B. To determine if there is a rise in abdominal venous pressure as intra-abdominal pressure is raised (Fig. 3).

Female fox terrier, 7.5 kilos. 5 per cent glucose, 500 cc at 5.00 P.M., May 23 and at 9.30 A.M., May 24, luminal, 0.12 gm. per kilo, at 10.00 A.M.; ether during operation only. 5 per cent acacia in 0.9 per cent saline used to raise abdominal pressure. Venous pressures recorded later in experiment by cannulas in right femoral and left external jugular.

Time.	Blood-pressure.	Abdominal pressure.	Urine drops per minute.	Conditions.
2.20 2.29	72	0	3	Control.
2.30	66	20	1	Acacia injection begun.
2.31	68	30	0	750 cc acacia injected; suppression.
2.35	82	30	0	Fluid held in abdomen.
2.37	90	15	1	Fluid released.
2.40	104	10	4	Recovery.
2.44	100	4	3	Recovery.
2.47	82	30	0	750 cc acacia injected; suppression.
2.52	110	30	8	50 cc saline intravenously (note diuresis).
2.54	102	40	0	More acacia injected into abdomen; suppression.
3.06	104	10	5	Recovery; pressure released.
3.07	96	15	3	Acacia injected slowly.
3.08	90	20	2	Injection continued; lag in output.
3.10	84	25	1	Injection continued.
3.15	84	28	1	Injected continued.
3.20	80	30	0	Injection continued; suppression.
3.28	88	28	1	Pressure released.
3.32	90	20	4	Recovery.
3.36	88	18	4	Recovery.
3.39	80	30	0	Acacia reinjected; suppression.
3.42	80	28	2	Pressure released.
4.20	98	8	3	Control; venous pressure: femoral, 6.9; jugular, 0.
4.25	52	28	0	Acacia into abdomen; venous pressure: femoral, 20; jugular, 0.
4.27	56	30	0	750 cc acacia injected; venous pressure: femoral, 24; jugular, 0.
4.29	74	12	1	Pressure released; venous pressure: femoral, 9; jugular, 0.

Experiment 3. To determine if pressure is raised in inferior cava at point where renal veins enter, as intra-abdominal pressure is raised.

Female mongrel, 5.2 kilos. Glucose 5 per cent, 500 cc at 5.00 P.M., May 26 and 10.00 A.M., May 27, luminal, 0.012 gm. per kilo. Saline used to raise abdominal pressure. No ether required.

Details of experiment were almost exactly the same as Experiment 2, and results entirely confirmatory.

Catheter used for recording pressure within inferior cava, connected to vertical tube, as manometer.

Abdominal pressure.	Catheter inserted (mm.).	Venous pressure (mm.).	Conditions.
4	2	3+	Control; catheter in femoral vein.
19	2	18+	Saline injected into abdomen.
19	10	18+	Saline held in abdomen; catheter pushed on.
19	20	18+	Same.
19	22	0	Blood flowed sharply out of tube.
16	5	0	Catheter in jugular vein; saline held in abdomen.
16	30	0	Catheter pushed on; saline held in abdomen.
16	33	12	Catheter tied in place and animal killed; tip of catheter in inferior cava just below the diaphragm; at 22 cm. from opening in femoral vein, tip of catheter was in inferior cava, just above diaphragm.

Experiment 4. To determine if there is a loss of tonicity of abdominal muscles when intra-abdominal pressure is gradually increased.

Female dog, 8.6 kilos, glucose 5.00 P.M. and 11.00 A.M. as usual. Anesthesia by ether only. Saline injected into abdomen, in 50 cc portions, allowing five minutes between injections. (No urine was excreted at any time during the course of this experiment.)

Total fluid.	Abdominal pressure.	Blood-pressure.	Conditions.
0	0.0	120	Control.
100	8.0	112	Sharp fall of blood-pressure followed second 50 cc injection.
500	10.4	116	Blood-pressure did not fall after subsequent injections.
1000	13.8	118	
1500	17.6	118	Abdomen very tense, but no dyspnea.
2000	26.4	120	No apparent change.
2100	30.0	120	Still breathing quietly.
2250	35.0	120	
2300	33.0	116	Fall in abdominal pressure and blood-pressure, with marked dyspnea; lower ribs bulging suddenly.
2350	36.0	114	Very marked respiratory distress.
2400	48.0	?	Blood-pressure fell sharply to zero; then infrequent, spasmodic heart beats and agonal respiration; recovery prompt on releasing pressure.

Conclusions. 1. A rise of intra-abdominal pressure to 30 mm. (mercury) is uniformly followed by complete suppression of urine in dogs; pressures lower than 15 mm. have no constant effect; from 15 to 30 mm., there is progressive diminution in rate of urine excretion. There is usually also a fall of 5 to 10 mm. in arterial pressure.

2. Venous pressure within the inferior caval system below the diaphragm rises with intra-abdominal pressure, and to almost the same extent.

3. Suppression of urine with high intra-abdominal pressure is probably due to the rise in abdominal venous pressure, the effects of which on the renal circulation are comparable to those of partial occlusion of the renal veins.

4. The fall in blood-pressure seems to be due to a temporary collapse of the inferior cava, until the venous pressure has risen to a point equal to intra-abdominal pressure.

5. When fluid is gradually introduced into the abdomen, the abdominal muscles lose their tonus, and much more fluid can be accommodated without pressure symptoms. The diaphragm is the last to yield, and its yielding is following by rapid circulatory failure, while respirations continue.

It is suggested that the loss of tonus in the abdominal musculature occurs as a means of compensating for ascitic collections which would otherwise raise abdominal venous pressure sufficiently to cause urinary suppression.

It is suggested that, since the rise of venous pressure resulting from the presence of an ascitic collection in the abdomen is limited to the venous circulation below the diaphragm, this may be a factor in the comparative limitation of the peripheral edema to the lower extremities in cases of inferior caval obstruction.

Dana and McIntosh[5] report a case of superior caval obstruction in which edema occurred chiefly in the face, neck and upper extremities; the lower extremities were not involved to any great extent in the edema. This should be contrasted with the inferior caval obstruction type of edema dealt with in the present paper.

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SIGNIFICANCE OF THE WILDBOLZ AUTO-URINE REACTION IN TUBERCULOSIS, WITH A REPORT OF 100 CASES.

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The tuberculin test has been regarded by many workers both in surgery and medicine as a certain sign of a tuberculous focus, but its limitations have been found and it is not now regarded as a complete automatic diagnosis but as an indication of the necessity for looking further.

Hence, when Wildbolz and his co-workers published that they believed it was possible to demonstrate the activity of a tuberculous process through the proof of antigens in the urine by means

of an allergy reaction of the skin, an added stimulus was given to the efforts to find a positive test which would demonstrate without any doubt the presence of an active tuberculous process.

Wildbolz and his co-workers worked on the theory that when there is an active tuberculous process in the body there must be products of disintegration due to the tubercle bacilli, and that these products of waste or disintegration are antigens or antibodies which are removed by the various secretory organs. The only question was whether the existence of these antigens could be proven.

Wildbolz assumed that if there was an active process in the body then there should be antigens excreted in the urine and that this urine, after certain modifications would, if injected intracutaneously, cause the skin to show infiltration and redness similar to that after the injection of tuberculin. If this reaction was positive then he assumed that as proof that the antigens were in the urine and also that there was an active process in the body producing these. If, however, the reaction was negative then it was assumed that this demonstrated that there were no areas of activity in the body.

Wildbolz stated further that the above reaction would not occur with urines from supposedly healthy individuals or from urines of persons with tuberculous processes that have been healed. Moreover, it never occurs unless the person gives a positive response to an injection of 1 to 10,000 dilution of tuberculin. Wildbolz first injected tuberculin in a patient to show whether the patient was allergic or not. Then he applied his auto-urine test when, if it did react, he was convinced it was proof of an active process in the person whose urine was used. Hence where there is an anergic person, that is one who would not react to his own urine, the test seemed to be of greater value inasmuch as it could be tried upon some other person who first reacted positively to tuberculin, because a person reacting to tuberculin would react positively to the auto-urine test. The reason for using the tuberculin test first was solely to show whether the person on whom it was performed was hypersensitive, or not.

In demonstrating the superiority of the auto-urine test over the tuberculin, Wildbolz demonstrated that the tuberculin response persisted unmodified for a much longer period than the response of the urine, which fades out completely in seventy-two hours. If the urine reaction persists after the clinical healing of the tuberculin process, then, said Wildbolz, we can be confident that there is some other condition present elsewhere. The specific nature of the urine reaction he demonstrated even more conclusively by the fact that after the subsidence of the urine reaction, if an injection of 1 to 10,000 tuberculin was injected near by, the apparently extinct urine reaction would flare up anew, the infiltration and redness becoming more distinct and more marked again.

The Auto-urine Test. In preparation of the auto-urine test, the first thing to consider is a method by which the antigens can be concentrated from the highly diluted urine in a sufficient quantity for demonstration without destroying the antigens, which are destroyed at a temperature of 60° C. The technic is as follows: 100 cc of morning urine is evaporated to $\frac{1}{10}$ of its volume, or 10 cc, in vacuo, at a temperature not exceeding 50° C. When the urine is concentrated to $\frac{1}{10}$ of its volume, the contents are placed in a sterile test-tube and allowed to stand for twenty-four hours. Then the contents are filtered through sterile filter paper impregnated with 2 per cent phenol. $\frac{1}{10}$ of a cubic centimeter of the filtrated urine is then injected intracutaneously on the anterior surface of the forearm, using exactly the technic of the Schick test. The reaction is manifested by a local infiltration and redness at the point of the injection, which develops within twenty-four to forty-eight hours after the introduction of the urine. The size of the infiltration varies from 5 to 15 mm. In every case a control is injected in the same manner and in the same quanity on the opposite forearm. The control being a 1 to 10,000 solution of tuberculin.

The theory of the auto-urine test sounds very plausible, but is it possible to prove that there is an active tuberculous process in the body by the injection of one's own urine, after certain modifications, and obtaining a response in a local reaction?

We know that the skin of certain individuals is more sensitive than that of others particularly so when these individuals have had previous infections such as tuberculosis, asthma, hay fever, etc. We know that these persons who display an intense reaction to foreign proteins always react to the skin tuberculin test. If this is so, then why should not these persons who react to proteins also react in the same way to the antigens supposedly thrown off in the urine after some infection other than tuberculosis, for if there are antigens given off in the urine from an active tuberculous process somewhere in the body, no matter how remote the focus may be, then there must also be antigens given off in the urine from other infections as well, as in pneumonia, typhoid fever, syphilis, staphylococcemia, and endocarditis? So if the urine from these persons is injected intradermally, why should it not show a similar reaction, and how are we to differentiate these reactions from each other?

In cases of apparently healthy individuals free from any sign or symptom of tuberculosis, I prepared a number of urines and found after injecting these that I obtained reactions similar to those who had tuberculosis. Certainly here there were no specific antigens to cause the reaction. In my series of healthy cases I became doubtful of the specificity of the auto-urine reaction and surmized that the reaction was the result of the traumatic and the chemical

qualities of the urine, and that while the urines of tuberculous persons may give a positive reaction, the same reaction may also be obtained from urines of non-tuberculous persons, sometimes on account of the presence of drugs in the urine, but also, in the absence of such a cause, from some unexplainable reason.

The reaction appears to depend not only upon the quality of the urine injected but also on the receptivity of the patient, as the same sample of urine may give a positive, doubtful, or negative reaction in various persons who are in a tuberculous allergic state.

On the whole, therefore, while the presence of antigens in the urine of tuberculous patients is a matter of scientific interest, no diagnosis, and still less an exact appreciation as to the activity of the disease or its clinical prognosis, can be based on this reaction.

According to Petersen, it has been shown that from the time of birth of the individual the organism begins to alter in the reactivity of the skin, which, at first negative to tuberculin, increases progressively with the age of the individual until in adult life a maximum is reached and maintained, but during this period not only does the skin become sensitive to tuberculin, but it becomes increasingly sensitive to a series of other bacterial and plant proteins and extractives as well. We are dealing with a more or less sensitization or allergy of the skin. This allergy may be a more or less specialized property of the skin or may be localized in certain areas of the skin. As a result of it the tissues acquire the ability to react more energetically and more promptly to outside stimuli, whether specific, as with tuberculins, or non-specific as when other proteins are injected in and about an area previously injected. The conclusions, therefore, is that in tuberculous individuals the skin and the body as a whole are hypersensitive not only to tuberculins but to proteins in general. It must always be borne in mind that when the injection is made a certain amount of tissue injury is done and that some of the cells may be injured both by the trauma and the toxic material injected.

From these observations it is apparent that non-specific factors can undoubtedly influence the tuberculin reaction or the other skin reactions, both in the sense of depressing and accelerating the reactivity of the skin.

In performing the auto-urine test in persons with suspected tuberculous processes, how would it be possible to demonstrate the presence of antigens in the urine if there is some renal impairment, for then the antigens would be in such a diluted state that it would hardly be possible to demonstrate their presence by a reaction in the skin? If there is a positive reaction, how can we be sure that the reaction is not due to some chemical substance in the urine that was not altered by the evaporation of the urine?

Reviewing the foreign literature on the subject, I found as follows:

W. Unverricht believed that the sensitiveness of the intracutaneous test is due to the larger area in which the tuberculin and the tissue react, and that the more rapid absorption of the tuberculin is in consequence of the greater pressure with which it is forced into the lymphatics. H. Eliasberg and E. Schiff conclude that the urine reaction may be specific, but it gives no proof as to the activity of the lesion. R. Offenbacher does not believe the test to be reliable, as in a number of instances the tuberculin test was positive and the auto-urine test negative. T. Arlong, Piery, Ledru and Codier consider that the auto-urine test does not differentiate between an active and an inactive lesion. E. Liebhard states that in his series of cases the urine reaction was not intense enough and was too inconsistent to be of great practical significance in its present form. Hanns concludes that an active tuberculous process does not preclude a negative intracutaneous reaction except in fatal rapidly-progressing cases. Parallelism between the intracutaneous tuberculin and the urine reaction was not established. On the contrary, a feeble allergy toward tuberculin was associated with a strong urine reaction and *vice versa*. O. K. Klercher attempted, by means of the intracutaneous test, to differentiate active from inactive tuberculosis, but without success.

G. Farrago and P. Randt conclude that the auto-urine reaction has no value whatsoever in the diagnosis of tuberculosis, as the reaction is due to certain chemical qualities in the urine and the question whether the urine of the tuberculous patient contains specific substances which are valuable in the diagnosis of tuberculosis remains for further investigation.

Reviewing the American Literature on the subject, I found only one article, written by C. B. Gibson and W. E. Carroll. This article working on the same line as Wildbolz worked, gives the data of some 40 cases but does not give conclusions either proving or disproving the efficiency of the auto-urine test.

However, Petersen in his new book on Protein Therapy disproves Wildbolz's statement that many patients with an active tuberculous process do not react to foreign proteins because they have an organic resistance or skin anergy. Petersen states that persons who have tuberculosis, hay fever, or other infections, show a skin allergy or skin hypersensitiveness due to the continual absorption of proteins and that these persons will react to almost every protein injected. This, obviously, is quite contrary to the Wildbolz statement.

Wildbolz also states that the auto-urine test is always negative in non-tuberculous patients, but in my series of cases I cannot agree with this statement as I found a number of healthy persons who gave a positive auto-urine reaction, due, no doubt, either to the hypersensitiveness of the skin, or to some chemical substances in the urine or to traumatism from the injection. The auto-

urine reaction was also positive in a number of cases where the tuberculin test was negative and *vice versa*.

Although I considered all these points I was determined to devote enough additional time to try to prove or disprove the efficiency of the auto-urine test for tuberculosis from the standpoint of activity. In my series of anergic cases I injected their urines into persons who were allergic, but found that the result was very inconsistent and unreliable. Neither did those of my injections which were positive flare up again after an injection of tuberculin. In only 5 cases did I get a systemic reaction, whether from the tuberculin or the urine I cannot say. All of the cases complained of a severe burning sensation after the injection of the urine and several had sore arms for a few hours after the injection. No burning sensation or sore arms were noticed following the tuberculin injections.

I was convinced that if this test was reliable, we had at last found something which was a step forward and which would shed some light on the subject of the activity of tuberculosis, all other tests for tuberculosis having been very disappointing and as indicators of activity, valueless.

But I found that the auto-urine test on the whole is one that cannot be performed on every person with the ease with which Mantoux or von Pirquet can be performed. In other words, it is not practical as it requires one who is familiar with the test and who has the time to devote to its preparation, which is considerable, due to the fact that the evaporation of the urines alone require at least one hour. One can readily realize in my series of 100 cases how much time was consumed in the preparation of the urines.

Summary of Results. 1. *Tuberculous Cases.* Result in 48 cases of tuberculosis: In 44 cases of active tuberculosis, 26 resulted in a positive reaction; 18 resulted in a negative reaction; 4 of the 48 cases were classed as inactive or arrested; 3 of these resulted positively and 1 negatively to the auto-urine test.

Cases.	Mantoux.	Auto-urine.
24	Positive	Positive.
8	Negative	Negative.
5	Negative	Positive.
11	Positive	Negative.

2. *Non-tuberculous Pulmonary Conditions.* Result in 24 cases: 14 of these 24 cases gave a positive reaction in the auto-urine reaction; 10 of these gave a negative reaction.

Cases.	Mantoux.	Auto-urine.
9	Positive	Positive.
3	Negative	Negative.
6	Negative	Positive.
6	Positive	Negative.

3. *Apparently Healthy Cases and Various Diseases.* Result in 22 cases: 11 resulted in a positive auto-urine reaction; 11 resulted in a negative auto-urine reaction.

Cases.	Mantoux.	Auto-urine.
13	Positive	Positive.
6	Negative	Negative.
0	Negative	Positive.
3	Positive	Negative.

4. *Allergic Cases with Positive Sputum.* Result in 6 cases: All but 2 patients were negative when their urine was injected into their own skins, but when it was injected into allergic persons, 4 of these gave a positive reaction.

Cases.	Mantoux.	Auto-urine.
0	Positive	Positive.
4	Negative	Negative.
2	Negative	Positive.
0	Positive	Negative.

Summary and Conclusion. 1. Healthy individuals and persons with non-tuberculous diseases may show a positive auto-urine reaction.

2. Persons with healed tuberculous processes may show a positive auto-urine reaction.

3. In allergic persons the auto-urine reaction has no practical value, as proven by inconsistent results obtained from injecting their urines into allergic persons.

4. The auto-urine reaction is not reliable since in a number of cases where the tuberculin test was positive, the auto-urine reaction was neagtive, and *vice versa.*

5. It is not practical for every day use.

6. The reaction appears to be due not only to the quality of the urine injected, but also to the receptivity of the patient, as the same urine may give a positive result in one person and a negative result in another.

7. A positive result is not proof that there are antigens in the urine.

8. In all probability this reaction is due to: The hypersensitiveness of the skin; to chemical properties in the urine; to the traumatism induced by the injection of the urine; to drugs in the urine.

9. From a study of the cases that I have presented I have arrived at the conclusion that the Wildbolz auto-urine test for active tuberculosis has very little, if any significance, in its diagnosis.

I wish to express may appreciation to Drs. A. L. Goodman and Jerome Leopold for their coöperation in making possible my work with the auto-urine test.

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REVIEWS.

CLINICAL DIAGNOSIS AND SYMPTOMS. By ALFRED MARTINET, M.D. Authorized English translation from the third, revised and enlarged edition. By LOUIS T. DEM. SAJOUS, B.S., M.D. Pp. 1388; 895 illustrations. Philadelphia: F. A. Davis Company, 1922.

THIS two-volume work by Martinet, which has been translated by the younger Sajous, offers to the practitioner a fairly thorough discussion of physical diagnosis, laboratory diagnosis and analysis of symptoms. To the reviewer the second volume which contains the analysis of the different symptoms seems to be of greater value than the first volume. The first volume, on the examination of the various organs and portions of the body, seems to be somewhat superficial and to deal with the subject matter non-critically. A certain amount of material in the book is many years old and has not stood the test of time. In the second volume, however, the author has taken up systematically a discussion of symptoms. These are arranged alphabetically and the reader can in a minute, with a minimum amount of difficulty, determine the causes of hematemesis or of hematuria or of jaundice, tremor or any other one of a host of symptoms. The book is profusely illustrated, largely with diagrams, which are well conceived and executed. It can be recommended most highly. M.

DISEASES OF THE EAR, NOSE AND THROAT. By WENDELL C. PHILLIPS. Pp. 881; 572 illustrations. Philadelphia: F. A. Davis Company, 1922.

IN the sixth edition, Dr. Phillips has eliminated much that is obsolete and introduced recent methods in audiometry, bronchoscopy and laboratory diagnosis.

The real test of such a work is its practical adaptability for use by student and practitioner. Its comprehensiveness, especially in minor detail, while somewhat confusing to the former group, will enhance its value to the latter. An increase in the number of basic anatomic illustrations in the nose and throat section would be helpful. The book is more compact in its present form and everything considered is one of our most valuable reference works. B.

PRACTICAL PHYSICS. By J. A. CROWTHER, Sc.D., F. Inst. P., University Lecturer in Physics, as Applied to Medical Radiology, Cambridge University. Pp. 260. London: Henry Frowde, Hodder & Stroughton, 1922.

THIS little book is essentially a laboratory manual for elementary students of physics. It comprises a series of simple experiments, such as are used for teaching in every physics laboratory, so clearly and concisely explained that no student should have difficulty in carrying the work assigned to a successful termination. Its scope is entirely limited to premedical teaching. A.

DIE LUMBALPUNKTION. By DR. MARTIN PAPPENHEIMER, Privatdozent, an der Universität Wien. Pp. 184; 8 illustrations. Wein: Rikola Verlag, 1922.

THE anatomy and physiology of the regions involved, the various methods of examination and their diagnostic, prognostic and therapeutic significance are discussed, in the hope of correcting the serious errors encountered by the author in text-books and in the minds of his acquaintances. W.

A KEY TO THE ELECTROCARDIOGRAM. By LOUIS FAUGERES BISHOP, M.A., M.D., Sc.D., F.A.C.P., Professor of the Heart and Circulatory Diseases, Fordham University, etc. Pp. 94; 43 illustrations. New York: William Wood & Co., 1923.

THE story of electrocardiography has been told simply and in a most interesting manner in this little book, which should be of special value to those who now know nothing of electrocardiography, wish to know something, but are unwilling to devote too much energy to the subject. The author is more optimistic as to the clinical value of electrocardiograms than most workers in this field. Several statements should not be permitted to go unchallenged. The author relates the waves of the electrocardiogram to contraction of the heart and states that the work of the ventricle is recorded by the T-wave. It was demonstrated long ago that the electrical disturbances in the heart precede contraction by measurable intervals and it is now pretty well established that the T-wave records, not work of the ventricle, but subsidence of the excitation wave. Too much dependence is placed upon the electrocardiographic evidence of disproportionate enlargement

of one or the other ventricle. The reviewer must dissent from the author's opinion that pulsus alternans is rare, and in view of the statement that he has no example of it in his collection of electrocardiograms, refers him to Fig. 20, page 49. W.

THE MEDICAL CLINICS OF NORTH AMERICA (VOL. VI, NO. 4). Pp. 831–1094. Philadelphia and London: W. B. Saunders Company, 1923.

THIS number contains twenty-six clinics from four of Philadelphia's largest hospitals, and numbers among its contributors McCrea, Riesman, Norris, Anders, Musser, Funk, and Pepper. The subjects dealt with vary widely, but there is, on the whole, a preponderance of clinics upon rare conditions, in which diagnostic difficulties afforded the chief interest. Probably to the average reader Pepper's Clinic to the first-year class in medicine, entitled "Diabetes Mellitus with Slight Acidosis: a Discussion of the Buffers of the Blood," and Torrey's discussion of "Aneurysm of the Aorta with Remarks Concerning the Effects of Aneurysm on the Coronary Circulation" will be of the greatest interest. A.

BIOMETRICAL STUDIES IN PATHOLOGY. I. THE QUANTITATIVE RELATIONS OF CERTAIN VISCERA IN TUBERCULOSIS. By RAYMOND PEARL and AGNES LATIMER BACON. Johns Hopkins Hospital Reports, Vol. XXI, Fasc. III. Pp. 72; Figs. II and tables 23. Baltimore: Johns Hopkins Press, 1922.

THIS third emanation from the Statistical Department of the Johns Hopkins Hospital attempts to arouse the medico's interest by considering man in the opening line as one of the higher Metazoa. In spite of the present popularity of biometrics, constitution clinics and such like, however, the pamphlet proved incapable of holding the reviewer's attention. With relief he found a summary of only two and a half pages and there read "the general problem with which this paper, which is the first in a series that as a whole will deal with this problem, is that of the adaptive organic regulation of the normal balance of the parts of the body, operating under pathological conditions." Fatigued by the endless quality of this sentence, he waded irresolutely through the six indices calculated from the data of 5,000 tuberculosis autopsies and the significant and insignificant negative and positive correlations deduced therefrom. When sufficient vigor had returned, he analyzed the analysis

and was rewarded in finding that "broadly speaking" no correlation was possible in several of the ratios selected; also that with increasing age the heart tended to be relatively heavier than the other viscera studied and that in active tuberculosis, the heart was relatively to those viscera lighter than in inactive tuberculosis. If the reader's interest is enough greater than the reviewer's, he will turn to the text for the significance of these important facts.

K.

REST AND OTHER THINGS. By ALLEN K. KRAUSE, A.M , M.D., Associate Professor of Medicine, Johns Hopkins University; Director, Dows Tuberculosis Research Fund, Johns Hopkins University; Editor, American Review of Tuberculosis. Pp. 159. Baltimore: Williams & Wilkins Company, 1923.

IN antituberculosis propaganda the author believes that more stress should be laid upon the universal practice of better hygienic habits. Heretofore almost the whole emphasis has been placed upon the well-nigh impossible task of preventing infection with the ubiquitous tubercle bacillus. He makes a plea for the establishment in our medical schools of tuberculosis foundations for purposes of more effectual study and teaching in this field. As in most collections of addresses upon one subject, there is considerable repetition, but the style is forceable, and in the field of tuberculosis the author speaks with undoubted authority. A.

CARRIERS IN INFECTIOUS DISEASES, A MANUAL ON THE IMPORTANCE OF PATHOLOGY, DIAGNOSIS AND TREATMENT OF HUMAN CARRIERS. By HENRY J. NICHOLS, M.D., M.A., Major, Medical Corps, U. S. Army; Instructor in Bacteriology, Parasitology and Preventive Medicine, Army Medical School, Washington, D. C. With a Section on, CARRIERS IN VETERINARY MEDICINE. By R. A. KELSER, D.V.M., M.A., Captain, Veterinary Corps, U. S. Army; in charge, Veterinary Laboratory, Army Medical School, Washington, D. C. Pp. 184; 11 illustrations. Baltimore: Williams & Wilkins Company, 1922.

THIS manual presents a fairly complete consideration of the subject of carriers. Unfortunately, the didactic rather than the monographic style of presentation detracts from the scientific value of the work by permitting the author to introduce personal convictions supported by an incomplete and rather hurried gleaning of the great volume of literature on this important phase of

preventive medicine. The section on carriers in veterinary medicine is freer from this than is that on human carriers, and constitutes a very valuable, as well as the first, summarized review of this subject in medical literature. It is to be deplored that the lessons learned from the experiences of the World War in regard to the seriousness of hemolytic streptococcus complications, especially in respiratory diseases, are not emphasized. The introduction of the term phorology may not meet with general acceptance.

S.

Die Pfeilgifte. By L. Lewin. Pp. 517; 75 illustrations Leipzic: J. A. Barth, 1923.

An exhaustive treatise on arrow poisons of all kinds, giving the results of studies and experiments extended over thirty years. The poisoned weapons of the Middle Ages, of India, the Malayan Peninsula, Australasia, Africa and North and South America are all passed in comprehensive review in a manner that makes the book of interest to physicians, naturalists, ethnographers and psychologists alike. If its information is accurate, an estimate beyond the ability of the reviewer, this book should long remain an authoritative one on this subject.

K.

Clinical Laboratory Methods. By R. L. Haden, M.A., M.D., Associate Professor of Medicine, University of Kansas, Kansas City. First edition. Pp. 294; 74 illustrations. St. Louis: C. V. Mosby Company, 1923.

"All discussion of the interpretation of results has been intentionally avoided. The book is in no sense a text-book." On the other hand, it accomplishes well the limited purpose that the author has striven for, namely, to present succinctly a series of "laboratory procedures which have been thoroughly tried out and found to give accurate results." It, therefore, should be of more value as a practical handbook than as a guide to the student of these topics. Going farther afield than clinical pathology in its narrower limits, the author has included chapters on the chemical examination of the blood and other tissues, serology, clinical bacteriology and histological technic that will make the book cover the immediate needs of most clinical laboratories.

Believing the book to be a good one, the reviewer may be permitted to call attention to a few minor desiderata: Goodpasture's oxydase should certainly accompany if not displace the older Schultz method; insufficient emphasis is given to the importance

of cyst detection in amebic dysentery; the discription of Wilbur and Addis' quantitative urobilin estimation in stools gives a different calculation from the authors', with resultant figures that are too high (most text-books, however, omit this test entirely!); the method for blood platelets is somewhat antiquated and should at any rate be supplemented by an indirect method; the authors' names on page 113 are incorrect; the inclusion of a thick smear method for malarial organisms would have been desirable. On the other hand, it is up to date in most particulars, has the earmarks of having been written by a capable worker, and the material is offered in very presentable form. The practice of frequently giving the author's reference immediately beneath the title of the test is commendable. Throughout the book are useful tables, presenting valuable information in concrete form, also several laboratory aids of the author's own devising. Altogether it constitutes a welcome addition to the clinical laboratory workshop.

K.

RULES FOR RECOVERY FROM TUBERCULOSIS. By LAWRASON BROWN, M.D. Fourth edition. Pp. 217. Philadelphia and New York: Lea & Febiger, 1923.

PROBABLY in no disease is a well-considered and well-administered plan of treatment more important than in tuberculosis, and probably nowhere in this country has the system of treating tuberculosis been developed to a higher grade of perfection than at Saranac. From this unique source of experience the author answers the patient's questions in his own language, and tells him not only what he must do to get well, but when and how and why. The book is valuable as a layman's handbook, and may be consulted with profit by the physician as well.

A.

MIND AND ITS DISORDERS. A Text-book for Students and Practitioners of Medicine. BY W. H. B. STODDART, M.D., F.R.C.P. Fourth edition. Pp. 592; with illustrations. Philadelphia: P. Blakiston's Son Company, 1922.

AS is to be inferred from the title, this is primarily a text-book on psychiatry rather than neurology. It is divided into three parts: Part I deals with "Normal Psychology;" Part II, with the "Psychology of the Insane;" and Part III, with "Mental Diseases." The book is refreshing in many respects. It gets away from the straight-laced classifications of many American

and German text-books of the period previous to the war. It shows a healthy appreciation of the best things contributed by the psychoanalysts, and of the contributions of such workers as Cannon, Sherrington and others; and, not least of all, it contains some practical though simple hints on usually neglected but necessary topics, such as Case-taking, General Treatment of the Insane and certain Medico-legal Procedures. The last topic, of course, is treated from the British point of view, but this does not discount its value from a general medico-legal point of view. Some of the best chapters under "Normal Psychology," are those dealing with Fatigue, Sleep and Dreams, the Sentiments, Language and the Ego. These are clearly written, brief and to the point. They show a familiarity with the best practical work of recent or current American and English psychologists of accepted standing. Under Part II there is a short chapter on Psychoanalysis. This chapter follows Freud pretty closely, but effectively avoids introducing discussion of material and methods that the best in Freudianism has already discarded. The paragraph on Technic is very explicit and helpful.

In Part III the classification of the Neuroses and Psychoneuroses follows Freud pretty closely. It is pleasing to get a chapter on the Paraphrenias, for which Kraepelin must, of course, be thanked. The chapter on Epilepsy is one of the best written in the book, with possibly the exception of the paragraphs on treatment. It is interesting to note that luminal is not mentioned. The so-called "Organic Insanities" are treated in a rather cursory manner, and evidently with not the same enthusiasm as exhibits itself in the earlier chapters of the book. Their extreme brevity gives one the feeling that perhaps this portion of the book had been better omitted entirely. For a compact, readable, dependable and useful manual of mental disorders, however, the reviewer feels that the beginner, as well as the so-called "busy practitioner," would have to search far to find better. J.

RADIO-DIAGNOSIS OF PLEURO-PULMONARY AFFECTIONS. By F. BARJON. Translated by JAMES ALBERT HONEIJ, M.D., Assistant Professor of Medicine in charge of Radiology, Yale School of Medicine. Pp. 183; 27 figures and 50 radiographs. New Haven: Yale University Press, 1922.

THIS volume is in five parts, taking up: (1) Methods of examination, (2) radiological study of the pleuræ, (3) bronchi, (4) lungs, (5) penetrating wounds of the thorax by war projectiles. The author has attempted one of the most difficult tasks in writing a

book on roentgen-ray diagnosis of chest pathology. Part II, dealing with diseases of the pleuræ, is admirably presented. The reviewer, however, feels that the volume is not complete, in that no study of conditions, such as pneumoconiosis and chest signs and pathology, caused by the inhalation of foreign bodies, is included. Then, too, there are quite a few eminent authorities that probably would feel that the chapter on pulmonary tuberculosis is rather weak. The book is well written, and the publishers deserve credit for the printing and the type of paper that is used in the book. The illustrations are fair. The reviewer strongly feels that if the translator were given the privilege of editing the book the weak points would be remedied. P.

NOTES ON MATERIA MEDICA, PHARMACOLOGY AND THERAPEUTICS FOR DENTAL STUDENTS AND PRACTITIONERS. By FRANK COLEMAN, M.C., L.R.C.P., M.R.C.S., L.D.S., Assistant Dental Surgeon St. Bartholomew's Hospital, Dental Surgeon Royal Dental Hospital, etc. Fifth edition. Pp. 308. London: Oxford Medical Publications, 1922.

THIS little book deals in a concise but reliable manner with the materia medica, pharmacology and uses of the principal drugs employed by the dentist. The names of some of the preparations, being in accordance with the British Pharmacopœia, will be unfamiliar to American students and practitioners. The book contains short chapters on vaccine therapy, organotherapy, electrotherapy and radiotherapy. I.

EXERCISE IN EDUCATION AND MEDICINE. By R. TAIT MCKENZIE, M.D., LL.D., Professor of Physical Education and Physical Therapy and Director of Physical Education, University of Pennsylvania. Third edition. Pp. 601; 455 illustrations. Philadelphia: W. B. Saunders Company, 1922.

THIS book is addressed to students and practitioners, to teachers of youth, medical and physical, hoping to give a comprehensive view of the space exercise should hold in a complete scheme of education and in the treatment of diseased conditions. Exercise has so many points of contact with education, and is so intimately related to mental, moral and social training, that a progressive educator is compelled to study its various phases.

In this, the third edition, the author has inserted the results gained from his experience as, Physical Training Officer in the

British Army at Aldershot, as Medical Officer in Command of Convalescent Camps and as Inspector in such camps in England, Canada and the United States. He shows the part that exercise bears on the treatment of "soldiers" heart; the place Swedish gymnastics has taken in discipling great masses of slow, awkward men in speed, accuracy and alertness. He further shows how the maimed and crippled were and can still be reëducated in their last coördination, their stiffened joints, shattered nerves and atrophied muscles.

Exercise has come to stay. Italy and France have been shown its advantage; England, Germany and Sweden already know it. In the United States already twenty-three states have made physical education part of their school program.

In this work the author shows in most convincing style his thorough knowledge of his subject, and presents it in a most interesting and instructive manner. We all should have the work not only for our patients but for our own use as individuals.

E.

NUTRITION OF MOTHER AND CHILD. By C. ULYSSES MOORE, M.D., M.Sc. (PED.), Instructor in Diseases of Children, University of Oregon Medical School; Medical Director of the Coöperative Infant Welfare Society of Oregon. Including menus and recipes by MYRTLE JOSEPHINE FERGUSON, B.S. in H.Ec., Professor of Nutrition, Iowa State College, Ames, Iowa. Pp. 227; 33 illustrations. Philadelphia and London: J. B. Lippincott Company, 1923.

THE reviewer welcomes a book on this most important subject which can be put into the hands of the young mother without feeling that she will be submerged in a maze of, to her, unintelligible scientific phraseology. The same feeling relates to the social worker and the visiting nurse. The author has brought out in a common-sense manner all that vital part of the advances of recent years in nutrition which is necessary for a full understanding of the subject. There is a short discussion of the former and the newer ideas on nutrition. Then a definite statement as to the three known vitamins, their value and their distribution in foodstuffs, and the effects of their omission from the diet. To obstetricians, especially, the chapter of diet during pregnancy and lactation will be of interest. The subject of the diet of the normal baby, of the premature infant, of the older child are gone into in detail. The book makes rather a point of prevention of disease through proper diet than as a book on treatment of disease. The two appendices contain information often sought for in vain in books on nutrition, and add to the usefulness of the book. W.

PROGRESS
OF
MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

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Results of the Treatment by Radiation of Primary Inoperable Carcinoma of the Breast.—LEE (*Ann. Surg.*, 1922, **76**, 359) says that primary inoperable carcinoma of the breast has shown good results by radiation. The type of radiation, however, must be properly selected for the individual case, while over-radiation must be avoided. The palliative operation following properly planned radiation is of service in well selected cases. The results to date are very gratifying and encouraging. As the disease itself and the technic of radiation become better understood, it is believed that more satisfactory results will follow.

Diagnosis of Early Breast Tumors: Based on their Clinical Picture or their Gross and Microscopical Picture at the Exploratory Incision.—BLOODGOOD (*Boston Med. and Surg. Jour.*, August 17, 1922, p. 243) says that more attention must be paid to history and to examination by inspection and palpation, first, to exclude the group in which operation is not indicated; second palpation of a definite lump must be developed to a method of greater precision; third, when tumors must be explored, surgeons must learn to recognize the benign type in which excision of the tumor with a zone of breast is sufficient for the protection of the patient. For the present, the mistake that should never be made is an incomplete operation for a malignant lesion. A mistake which is and must be made in a certain group ol benign lesions hard to recognize, is the complete operation. The author feels that trained surgeons can and do recognize cancer of the breast at exploration and also the distinctly encapsulated adenoma and blue-domed cyst.

Autogenous versus Heterogenous Bone Pegs.—TAEMOWSKY (*Surg., Gynec. and Obst.*, 1922, **35**, 342) says that the clinical behavior of a beef bone graft depends entirely on the relative activities of the osteoblasts and osteoclasts. With proliferation of new cells from the living proximal and distal ends of the fractured bone keeping pace with absorption

of dead cells from the graft, complete disappearance of the latter coincides with complete union of the fracture or filling-in of defect. With hyperactive new cell formation and sluggish absorption, the graft constitutes a sequestrum which either eburnates and remains in a state of quiescence or acts as an irritant foreign body with sinus formation and periodic extrusion of dead bone spicules. With hyperactive bone absorption and sluggish new bone formation, the graft disappears by combined extrusion and absorption before union or filling-in of defect has taken place. The factors which enable us to attain the ideal, *i. e.*, an even balance of absorption and proliferation are: (1) The thorough trimming off of dead bone proximally and distally with curette and chisel; (2) firm approximation of the bone graft to living bone; (3) absolute asepsis. Finally, it has seemed to the author that the term infection is used too loosely—it is in truth, rapid necrosis of the graft without true infection. In other words, subacute osteomyelitis with no antibody reaction on the part of the individual, should not be classed as an infection, but as an ordinary tissue necrosis.

The Cause of Certain Acute Symptoms Following Gastro-enterostomy.—HADEN and ORR (*Johns Hopkins Hosp. Bull.*, 1923, **34**, 26) says that the symptoms and chemical findings (in a short series of patients showing severe reaction after gastro-enterostomy) were characteristic of intestinal obstruction. The authors attribute the symptoms to absorption of poison, probably formed in the duodenum following gastro-enterostomy. These patients showed a high level of non-protein nitrogen of the blood, low blood chlorides and suppression of chloride excretion following gastro-enterostomy. Marked alkalosis was noted in 1 patient; two had a CO_2 combining power at the upper limit of normal when first determined. Very high nitrogen excretion in the urine was also noted. All patients presented clinical symptoms of a severe intoxication, with laboratory findings characteristic of upper intestinal tract obstruction. It is probable that some duodenal obstruction at the site of gastro-enterostomy interferes with drainage of the duodenal loop.

The Lymph Nodes in Carcinoma of Rectum.—McVAY (*Ann. Surg.* 1922, **76**, 755) says that rectal carcinomas are the most common form of intestinal neoplasms and make up 4 per cent of all cancers of the body. The majority of patients are in the sixth decade, with males predominating slightly. The location of the growth on the rectal wall varies. About as many occupy the anterior wall as the posterior, with the greatest number of growths from the ampulla to the rectosigmoidal junction. Adenocarcinoma is the commonest type. Metastasis to the glands usually takes place slowly and the liver is the organ most affected, by secondary growths. The size of the growth in the rectum cannot be relied upon as an accurate index of probable lymphatic involvement. Growths without lymphatic involvement, tend to grow into the lumen of the bowel. Growths with slight lymphatic involvement, tend to spread by direct extension and are slow growing. Carcinomas of the rectum with extensive lymph-glandular involvement, tend to metastasize through the lymph stream early. Metastastic lymph-glandular

involvement can only be definitely determined by systematic microscopical study of all the regional lymph nodes. The size of the lymph node is not an efficient means of determining whether or not there is metastatic involvement.

Intussusception.—ELLARS (*Am. Jour. Surg.*, 1922, **36**, 307) says that intussusception is noted with greatest frequency in children less than one year old, the incidence of the abnormal occurrence gradually decreasing as age advances. It is not a disease *per se*, the intestine ordinarily being normal when invagination begins, later becoming pathological because of strangulation and consequent interference with its blood supply. The actual determining etiological factor of intussusception appears unknown, but there are several anatomical peculiarities incident to infantile life which may be operative as predisposing or contributing causes. All medical and so-called mechanical methods suggested in the treatment of intestinal invagination are unwarranted, for they court disaster. Young children are not invariably unfavorable subjects for operative surgery. The tremendously and unreasonably high mortality of intussusception can be materially reduced by early diagnosis and prompt application of rational surgical principles.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

NEW YORK,

AND

CHARLES C. LIEB, M.D.,

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Voluntal, a New Hypnotic.—MILTNER (*Deutsch. med. Wchnschr.*, 1923, **49**, 73) reports that voluntal (tri-chlor-ethyl-alcohol-urethane) has proved, in his hands, an unusually safe and satisfactory hypnotic. It is almost tasteless and is readily administered in water, in which it is freely soluble. It produces a short stage of drowsiness followed by a deep, quiet, dreamless sleep from which the patient awakens fully refreshed. There is apparently a total absence of disagreeable after-effects, such as disturbance of digestion, headache, lassitude, dizziness, etc. No evidence of cumulation was encountered in his rather wide experience of prolonged administration. The hypnotic dose is 0.75 gm., but the factor of safety is apparently large, for no serious or even disagreeable symptoms were noted by the author when he took 2.5 gm. Like most of the other aliphatic hypnotics, voluntal fails to induce sleep in the presence of pain, severe cardiac dyspnea, etc. It is, however, a safe and powerful hypnotic, and in effectiveness stands midway between carbromal (adalin) and barbital (veronal).

The Treatment of Pernicious Anemia.—Though nothing is definitely known of the true cause of pernicious anemia, ROSENOW (*Klin. Wchnschr.*, 1923, **2**, 24) declares that there is little doubt that there is an enormous increase in the destruction of red blood cells and that the regeneration of the erythrocytes by the bone-marrow is quantitatively and qualitatively defective. Therapy may, accordingly, be directed toward decreasing the excessive destruction of the red blood cells or toward stimulating their formation in the bone-marrow. The "hemotoxin" is probably elaborated in the alimentary canal, and many measures have been suggested to limit its production. Rectal and colonic irrigations, as well as those *via* the duodenum, are usually unsuccessful in combatting the formation of the "hemotoxin" or in lessening the severity of any of the symptoms. Certain agents have been recommended as adsorbents of the toxin, but they do more harm than good, since they interfere greatly with the action of the intestinal enzymes. Glycerine and cholesterine have been tried and discarded. Cultures of various bacteria have proved disappointing, despite the abnormal intestinal flora. Such radical operations as the establishment of an artificial anus and subsequent irrigation of the intestinal canal through the artificial opening are of but temporary benefit. One of the most trying features of the treatment of pernicious anemia is the selection of a diet which appeals to the patient and supplies a sufficient number of calories. The anorexia, which is so common, does not yield to bitters, but may disappear after the prolonged use of hydrochloric acid. Large doses of the acid (with or without pepsin) are called for and are most beneficial in the presence of achylia gastrica. A diet rich in protein seems to promote red blood cell destruction, while a diet rich in fats does not. Diseases of the mouth are common and demand careful treatment; glossitis is best treated with tincture of myrrh or some other simple mouth wash; pyorrhea alveolaris and carious teeth are handled along dental lines. Of the drugs that have been tried in pernicious anemia, arsenic is unquestionably the best. It probably does not act directly on the bone-marrow, but acts indirectly by hastening blood destruction and thus inducing an active erythrocyte production. Arsenic may be administered either by mouth or parenterally. For oral use Fowler's solution is the most popular; it is customary to begin with small doses (3 drops three times a day) gradually increasing to full therapeutic amounts (30 drops thrice daily). Arsacetin (0.05 gm. three times a day) has no advantages over Fowler's solution. All arsenic preparations administered by mouth should be given after meals to minimize the local irritation. The arsenic must be continued for months or until saturation is reached; the most common symptom of saturation is paresthesia of the palms and soles. Habituation is readily induced in some patients, so that very large doses are not followed by poisoning. Parenteral administration of arsenic has no advantage over oral. Cacodylate of sodium is less active than Ziemssen's solution (1 per cent sodium arsenite) and is not advised. Atoxyl is altogether too dangerous to warrant its employment. Arsphenamine enjoys no special advantages unless the anemia is associated with lues. Roentgen-rays and radioactive substances are powerful stimulants of the bone-marrow. Thorium-X is more active than radium and is to be preferred. Small "stimulant"

doses may be given two or three times a week for a month or two. Iron has always proved quite worthless. Intramuscular or intravenous injections of blood have not proved as helpful as was anticipated when they were first introduced. Extirpation of the spleen is sometimes followed by brilliant results, but the benefit is only temporary. While none of the procedures discussed is curative, some seem to induce remissions and thus prolong life. Among the most valuable measures are arsenic, intramuscular injection of blood and the drinking of thorium-X waters.

The Action of Camphor, Menthol and Thymol on the Circulation.—The reports of the effects of camphor as a circulatory and cardiac stimulant are so contradictory that HEATHCOTE (*Jour. Pharmacol. and Exper. Therap.*, 1923, **21**, 177) deemed it worth while to attempt to clear up the confusion. Thymol is extensively employed in the treatment of ankylostomiasis and is reported to have led to occasional serious circulatory collapse. Menthol is related to camphor chemically and is included in the study for the sake of comparison. It was found that all three drugs (camphor, thymol and menthol) depress the isolated heart of the frog as well as that of the rabbit, and that this effect is due to a direct depression of the cardiac muscle. The strength of the beat is much more affected than the rate of the contraction. None of these drugs acts as an antidote to chloral, and a heart depressed by chloral is further depressed by the perfusion of any one of these drugs. Of the three, camphor is the least toxic and thymol probably the most. The coronary bloodvessels are dilated by all three—least by camphor and most by thymol. In anesthetized animals, camphor in non-convulsive doses does not cause a rise in blood-pressure, whether administered intramuscularly or subcutaneously. In animals deprived of cerebral hemispheres, no rise of blood-pressure is produced by huge doses (1 gm. per kilo). Even such small doses as correspond to those used in clinical medicine, caused a fall in pressure (15 per cent). The lowering of blood-pressure is ascribed chiefly to the depression of the heart muscle, and only to a minor degree to the relaxation of the bloodvessels. There is, therefore, no convincing evidence that camphor possesses any value whatsoever as a cardiac or circulatory stimulant. The unpleasant effects that sometimes follow the administration of thymol are due chiefly to a direct depression of the heart muscle, which is much more marked than with camphor.

On the Sensitivity of Different Nerve Endings to Atropine.—Textbooks on pharmacology frequently state that atropine depresses or paralyzes the nerve endings of the parasympathetic nervous system and the clinician is led to believe that this action is induced by ordinary therapeutic doses. According to HENDERSON (*Jour. Pharmacol. and Exper. Therap.*, 1923, **21**, 99), this is not the case; indeed, the usual therapeutic dose of atropine slows the heart by stimulation of the vagus center and the vagus endings are not paralyzed. He accordingly determined the amounts of atropine necessary to depress the ends of the bulbosacral autonomic outflow and ascertained the amounts necessary to cause so complete a paralysis of the various nerve endings that nerve stimulation with an induced interrupted current became

ineffective. The nerve endings are depressed in the following order: Nasal, chorda secretory, cardiac vagus, tonus of pyloric sphincter and small intestine, bladder, oculomotor to the pupil, salivary vasodilator, vagus to intestine for rhythmic and peristaltic movements. The endings are paralyzed in the order: Cardiac vagus, chorda secretory, chorda vasodilator, intestinal vagus. The endings in the bladder cannot be completely paralyzed. In man it was found that 0.2 mgm. caused a decrease in nasal secretion but not marked drying of the mouth, while 0.3 mgm. dried the mouth. This amount relieved griping produced by aloes. Two milligrams are required to increase the heart-rate to 150; this dose caused a submaximal dilatation of the pupil.

The Action of Certain Depressant Drugs on the Sensory Threshold for Faradic Stimulation in Human Subjects and the Effect of Tobacco-smoking on This Action.—HALE and GRABFIELD (*Jour. Pharmacol. and Exper. Therap.*, 1923, **21**, 77) used the Martin method for determining the effect of the diethylbarbituric acid hypnotics, of antipyrine and of acetphenetidine upon the sensory threshold for faradic stimulation. Parallel observations were made when the subjects were smoking and when they were not. In non-smoking experiments, the barbitals produced a slight transitory decrease in irritability; antipyrine showed its maximum effect at the end of half an hour, when it had decreased irritability by 30 per cent; acetphenetidin was somewhat more depressant, but its greatest effect was not shown till about ninety minutes after its ingestion. In all 3 cases, smoking tended to nullify the effects of these drugs, bringing the threshold observations within normal limits.

PEDIATRICS

UNDER THE CHARGE OF

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Physiology of Exercise in Children.—SEHAM and SEHAM (*Am. Jour. Dis. Child.*, 1923, **25**, 1) publish the result of their observations on normal children of school age. They found that the pulse rate in the standing position is invariably higher than in the lying position, the ratio being 1 to 15. The systolic blood-pressure in the lying posture is invariably higher than in the standing posture. The ratio of the blood-pressure in the lying posture to that in the standing equals 1 to 11. The ratio between the systolic blood-pressure in the lying and standing postures is about equal to the ratio between the pulse rate in the standing and the lying postures. All forms of exercise produce an increase in the pulse rate and the blood-pressure, the increase depending mainly upon the type of exercise. Neither the amount of exercise nor the speed determine the time of maximum reading. In the majority of cases the increase of the pulse rate and the blood-pressure as well as the reaction

time of the blood-pressure are in direct proportion to the speed and the amount of work performed. Height and weight do not influence the maximum physical output. The maximum physical output is in direct relationship to age, circumference of the chest, circumference of the thigh and the vital capacity. Two formulæ have been computed for calculating the maximum physical output with age as the basis. The first formula, applying to children six to seven years of age, is 1000 (5.45 age minus 25.3). The second formula, applying to children from eleven to fourteen years of age, is 3000 times the age. In exhaustive exercise on the ergometer, the increase of pulse rate varies from 48 to 116 beats irrespective of age. It is not necessarily parallel to the amount of work performed. In exhaustive exercise the rise of blood-pressure is proportional to the increase of work in about 50 per cent of the experiments. The average rise in blood-pressure after exhaustive exercise equals 31 mm. in children aged from six to nine years and 35 to 41 mm. in children who are older. The maximum rise equals 57 mm. and the minimum rise equals 16 mm. In 88 per cent of all the determinations made, the maximum reading of the systolic blood-pressure was seen within thirty seconds, and 12 per cent in from thirty to sixty seconds. In only 2 cases of the entire series was there a true delayed rise. In these experiments delayed rises did not occur after exhaustive exercise nor as the result of "temporary heart insufficiency." The reaction of the pulse is too long to be of any clinical value, as very few pulse rates return to normal within ten minutes. In general the reaction time of the systolic blood-pressure increases with an increase of work. There are exceptions to this.

The Action of Atropine on the Stomach of Infants.—Salomon (*Monats. f. Kinderh.*, 1922, **24**, 75) found that atropine lowers the tone of the stomach in infants and slows peristalsis. It does not alter the secretion of acid, nor act on the pylorus. The favorable results of large doses of atropine in the treatment of pylorospasm depend on its action on the musculature of the whole stomach. While a normal infant shows a reddening of the scalp after 1 to 2 drops of a 0.1 per cent solution of atropine sulphate when it is indicated, as in vagotonia, the infants may tolerate much greater quantities, and as much as 6 to 8 drops six times a day. Atropine very frequently gives excellent results in the habitual vomiting of infants.

Nutrition and Growth in Children.—Emerson (*Bost. Med. and Surg. Jour.*, 1923, **188**, 8) says that the forces affecting a child's health, which must be coördinated in order to secure success, are the home, the school and other agencies, medical care, and the child's own interest. The following program is suggested: Weighing and measuring as a means of identification; diagnosis based on complete physical growth, mental and social examinations; removal of physical defects as a prerequisite for successful treatment; measured feeding or a forty-eight hour diet record; mid-morning and mid-afternoon lunches; mid-morning and mid-afternoon rest periods; regulation of physical, mental and social activities; nutrition classes for the treatment of malnutrition; nutrition diagnostic clinics for problem cases; and average weight for height as a minimum standard of nutrition and growth.

Simple, Practical Method for Feeding Infants.—COWIE (*Mich. State Med. Soc. Jour.*, 1923, **22**, 10) states that the normal infant requires 45 calories per pound or 100 calories per kilogram of body weight to maintain its weight. After determining on 1 ounce of sugar as a constant factor, and accepting all sugars as containing 120 calories to the ounce, it becomes a very simple problem to know how much milk was necessary for the balance of the daily food. For example, if an infant weighed 10 pounds, he would require 10 times 45 minus 120, or 330 calories, which must be supplied in the milk. If there are 21 calories in an ounce of milk, 330 divided by 21 equals 15½ ounces as the amount of milk necessary to balance the energy requirements.

The Colloidal-gold Reaction in Acute Poliomyelitis.—REGAN LITVAK and REGAN (*Am. Jour. Dis. Child.*, 1923, **25**, 76) studied 42 cases of acute poliomyelitis, in which a study of the colloidal-gold reaction was carried out on 132 specimens of spinal fluid. There was always a reaction of colloidal-gold solution in the case of every poliomyelitic fluid taken during the acute stage of the disease. This reduction was constantly in the same zone; the zone of low dilutions or the so-called syphilitic zone. In 88 per cent of the spinal fluids examined, the reaction occurred in the first six dilutions between 1 to 10 and 1 to 320. In 14 spinal fluids the reaction extended to the seventh dilution, 1 to 640. These patients more or less characteristically presented marked polyneuritic or meningitic symptoms or else pronounced paralysis. The average curve or reaction showed very similar characteristics in the first and second weeks of the disease. A gradual decline in the curve was then noted. In no instance was a normal reaction encountered before the end of the third week of the illness. In 23 patients the spinal fluid was examined as late as the eighth week, and 15 or 65 per cent had become normal by that time. Cases in which a normal reduction returned early, from the third to the seventh week, were mild types of the disease, while those in which the curve remained elevated beyond the eighth week had usually polyneuritis or extensive and slowly improving paralysis or both. The reaction showed no distinctive points in the fatal cases, and therefore was of no value in prognosis in this regard. The positive reaction bore no constant relation to the presence of globulin in the spinal fluid nor to its disappearance. There was no close ratio between the number of cells per cubic millimeter in the spinal fluid and the test, but as the cell count decreased the colloidal-gold curve subsided, but somewhat more slowly, remaining elevated for several weeks after the cell count was normal. With the subsidence of the colloidal-gold curve there was usually an accompanying improvement in the patient's general condition, the paralysis, the meningitic symptoms, and the polyneuritis. It would seem that the return of a normal reduction of colloidal gold indicates approximately the end of the acute stage of the disease. As this coincides with the improvement noted clinically, this termination of the acute stage can readily be determined by watching the symptoms. In differential diagnosis the colloidal-gold reaction should be utilized in conjunction with history, symptoms and other laboratory data.

Evidence of the Necessity for a Bacteriological Standard for Grade "A" Milk.—MATLICK and WILLIAMS (*Jour. Hyg.*, 1922, **21**, 33) show the result of two farms producing milk of very different types although both were working under the same system of licensing. In neither case did the results compare with those obtained on a certified milk farm. Similar results were found to occur on certified milk farms when they first undertook production of this type of milk. They are due to the fact that the workers on the farms have to be trained in methods that are necessary for success. The certified farms have in the past been few in number, and have been under the control of those who are very anxious to produce a satisfactory result. These facts coupled with the fact that there is an official bacteriological standard to which the milk must attain, have made it possible to secure efficiency as time went on. There is no official bacteriological standard for Grade "A" milk, so that stimulus to better production is lacking and should be provided. In view of the difficulty, which is sometimes found in bringing the standard of labor on a farm up to the required level, the authors feel that evidence that milk of the required standard of cleanliness is being produced, should be made a condition of licensing. If this is not done, there is a danger that milk not of the required standard of cleanliness may be sold as Grade "A" milk. In that case the consumer may find that the keeping qualities of this milk are no better than those of milk that had previously been purchased. If this is done, grave harm may be done to the milk industry, which is endeavoring to supply the public with milk of uniform quality.

OBSTETRICS

UNDER THE CHARGE OF

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Rupture of the Uterine Peritoneum with Premature Separation of the Placenta.—EUFINGER (*Monatschr. f. Geburts. u. Gynäk.*, 1922, **59**, 158) describes a case of a multipara who during the first part of labor developed symptoms of separation of the placenta. A physician summoned applied a tampon and brought the patient to the hospital, where she was admitted in a very weak condition. Movements of the child and heart sounds could not be found. Section under local anesthesia was immediately undertaken. On opening the abdomen there was a large quantity of fluid blood. The placenta had almost entirely separated and the patient died shortly after the operation from acute anemia. At the autopsy a longitudinal laceration of the peritoneal coat of the uterus was discovered which penetrated through the upper muscular layer. A considerable part of the bleeding had come from this. On examination it was found that the process known as necrobiosis was present and that blood extravasated when the

placenta began to separate had dissected and weakened the muscle fibers. Much of the hemorrhage had come from the rupture of the peritoneum and muscle.

Excretion Through the Mammary Gland.—In the *Journal of the American Medical Association*, February 24, 1923, p. 557, is quoted the result of researches by Taylor concerning the composition of milk. In addition to the group of products manufactured *de novo* in the mammary gland, various substances are present which are also found in the blood and other fluids of the body of the animal. Among these are the so-called non-protein nitrogenous extradines, among which are the amino-acids, urea, creatin, creatinin and uric acid. Very frequently the blood has the same non-protein content as milk. Taylor has presented additional evidence that in the case of a warm-blooded animal during lactation, there is a definite relation between the usual output of nitrogen in the urine and the percentage of non-protein nitrogen in the milk. Both of these apparently depend upon the amount of protein taken in the food. In the blood are found the non-protein nitrogenous catabolites, and their concentration seems to determine the amount excreted in the urine and the percentage present in the milk. There is a distinct function of the mammary gland in this matter and waste non-protein nitrogenous substances evidently pass from the blood to the milk. The degree of concentration in the blood of the end products of protein metabolism determines the percentage in which these substances are found in the milk. When this function of the mammary gland is considered, it may readily be seen that a condition may arise wherein the milk may contain substances which make it unfit for food.

The Treatment of the Pyelitis of Pregnancy.—Rosinski (*Monatschr. f. Geburts. u. Gynäk.*, 1922, **60**, 116) calls attention to the fact that pyelitis complicating gestation may sometimes end fatally. In these cases fever develops soon after labor, which may be rapid and comparatively easy. The fatal issue is often seen about the tenth day after the labor. While it is true that these occurrences are comparatively rare, the author recalls four instances in which the patient became critically ill. The first was a primipara at five months taken suddenly ill with high temperature, two weeks of general medical treatment produced no improvement and the patient's strength failed rapidly. On admission to hospital she was stuporous, complaining of headache. There were symptoms of marked irritation of the peritoneum. The abdomen was distended, the patient vomited frequently and the tongue was dry, there was high fever and rapid pulse. Six days' hospital treatment produced no improvement and therapeutic abortion was practised, followed by recovery. This case occurred twenty-two years ago and the subject of pyelitis was not as commonly understood as at the present time. The second case was that of a young primipara at seven months with high fever, irritation of the peritoneum, slight jaundice and pain in the right hypochondrium. A diagnosis of gall-stones was made and operation was considered, this was declined although the patient was critically ill. The uterus was emptied and the urine obtained by catheter was loaded

with leukocytes. The recovery of the patient followed the termination of pregnancy. His third and fourth cases were similar in severity and recovered after the uterus was emptied. The writer discusses nephrotomy and admits that this deals efficiently in the acute danger, but it leaves the patient with a kidney fistula from which recovery may be long and tedious. Should pregnancy be interrupted after nephrotomy, conditions would not be favorable for healing. In his experience the pyelitis of pregnancy is seldom severe, simple treatment is usually sufficient for these cases, but where the condition becomes threatening the uterus should be emptied. The author describes the case of a young, vigorous woman who during her first pregnancy suffered from pyelitis with high temperature, during the puerperal period the condition of the urine did not greatly improve. The patient suffered little if at all and received no specific treatment for the condition. In the second pregnancy pyelitis recurred more severely and with great pain in the right hypocondrium. When labor came on pain becomes so severe in the region of the right kidney as to require the use of morphine for several days. On the third day of pain three small phosphatic stones were passed. In the third pregnancy the pyelitis became so severe that after a very excessive attack of pain, pregnancy was interrupted at the fourth month.

The Practical Significance of Affections of the Kidneys and Abnormal Conditions of the Urine in Pregnancy.—Fink (*Monatschr. f. Geburts. u. Gynäk.*, 1922, **60**, 229) has studied 215 cases of pregnant women in whom there was some abnormal condition of the kidneys and also an abnormal urine. He believes that the pathology of the kidney in pregnancy divides the condition into three groups: (1) That known as the albuminuria of pregnancy; (2) the nephropathy of pregnancy; (3) the various forms of acute and chronic nephritis complicating pregnancy. The albuminuria of pregnancy is characterized by the presence of serum albumin and hyaline casts of no great number in the urine, and this condition is practically without serious danger to the patient. It is not a disease but the result of the increased susceptibility of the epithelia of the urinary tubules to blood-pressure and altered conditions. This state is to be distinguished from more serious conditions by the absence of edema, increased blood-pressure and other symptoms which are clearly present in more critical states. The so-called pregnancy nephropathy, by some called the kidney of pregnancy, the nephritis of pregnancy and the nephritis of the pregnant, is not a primary kidney affection; it is an edematous state which reflects a similar condition throughout the organism and in common affects the condition of the kidneys. In these cases there is abundant albumen and many casts are in the urine. The principal symptom which distinguishes this from the foregoing, is the presence of edema. This process may go to the point of causing increased blood-pressure and hematuria. From these indications it is natural to treat these patients by limiting carefully the amount of water taken and by giving food which is not rich in water and also in salt. Only those cases which are most acute and accompanied by very high blood-pressure become dangerous, and in these patients eclampsia often develops. Such cases demand hospital treatment. Acute

nephritis at any stage of pregnancy is readily distinguished from nephropathy by a careful study of the history. They should be treated during the pregnancy by methods usually employed, with the omission of hot baths. It may be difficult to distinguish them from acute and violent cases of nephropathy but the condition of the blood-pressure should in this particular be of great assistance. Chronic nephritis in pregnancy gives the characteristic history, the long continuance of albuminuria, the presence of many casts and blood in the urine, the presence of fatty casts, of fatty elements in the urinary sediment, chronic headache, increased blood-pressure, a weakened action of the heart, disturbance of vision and cachexia. These cases demand very careful observation and thorough and efficient treatment. Nitrogenous food should be largely withdrawn, blood-pressure and action of the heart should be controlled and the examination of the eye grounds should be utilized as a valuable means of prognosis and the choice of treatment. This condition may clearly indicate the premature interruption of pregnancy.

Roentgen-ray Pictures as a Means of Teaching the Mechanism of Labor.—WARNEKROS (*Monatschr. f. Geburts. u. Gynäk.*, 1922, **59**, Heft 1–2) contributes a paper drawing attention to the value of this method of illustration in teaching the mechanism of labor. His article is somewhat in reply to a discussion or criticism of Sellheim, who has called attention to the fact that during labor the tissues of the child are subjected to unusual stress and therefore cannot give an accurate picture of conditions present. He illustrates with reproductions of roentgen-ray pictures showing unusual positions of the fetus and drawing attention to the fact that the whole fetal mass is elongated and very much compressed in its progress through the birth canal. The roentgen-ray pictures taken and copied by the author very little resemble those drawn ideally in text-books and are of interest as showing the degree to which the fetus is subjected to pressure during parturition.

An Unusual Complication in Twin Labor, the Entrance of both Heads into the Pelvis.—Described by MAHNERT (*Monatschr. f. Geburts. u. Gynäk.*, 1922, **59**, Heft 1–2). The patient in her second labor, aged twenty-nine years, believed herself to be at normal termination of pregnancy. Membranes ruptured without pains which afterward developed and midwife was called. The head of the child was spontaneously born but the remainder of the child, in spite of strong pains and strong contractions of the uterine muscle, was not delivered. Shortly after the birth of the head, the child died. On admission to hospital the mother's temperature was elevated, pulse 120, uterus was in firm contraction, the urinary bladder distended above the symphysis, a contraction ring in the uterus could not be made out. No heart sounds were heard nor could fetal parts be clearly distinguished. The head, already born, lay with the face directed posteriorly. The mucous membranes of the vagina and tissues about the urethra were edematous and suffused with blood. With the catheter 400 cc of cloudy albuminous urine was evacuated. While preparations were made to examine the patient, thoroughly, she had

a chill followed by a rise of temperature to 104° F. On examination the membranes of a second fetus containing a little amniotic liquid were detected; the head, with the sagittal suture transverse and occiput behind, was wedged upon the pelvic floor. The chest of the first twin was firmly wedged against the symphysis by the head of the second. Further spontaneous birth was impossible and as both children were dead the remaining membranes were ruptured and the head in the pelvis was perforated, the brain evacuated, and an effort was made through traction upon the head to deliver the second child; this failed and it was necessary to perforate the cranial bones of the second child, and to crush the tissues extensively before its body could be delivered. The perforated head of the second was then extracted by strong forceps. There was profuse postpartum hemorrhage and the placenta was removed manually shortly afterward. On examination of the bodies of the twins, both female in sex, the pressure upon the thorax of one by the head of the other was distinctly evident; at this point the skin was pallid, the neck deeply colored, giving the impression of congenital enlargement of the thymus or thyroid. The first child was 52 cm. in length. The second had also a congenital thyroid enlargement but otherwise well developed, 48.5 cm. long. The placenta was duovular. On measuring the pelvis it was not contracted. The puerperal period was complicated by four severe chills and fever lasting for six weeks with cystitis and pyelitis. On the twelfth day the patient passed urine involuntarily, and a fistula developed between the bladder and the cervix. This was subsequently corrected by operation, and three months after the labor the patient was discharged from the hospital in good condition. The author has collected a number of cases similar to this in the literature, and evidently the importance and severity of the complication will depend considerably upon the size and development of the children. The simultaneous engagement of twins with one child in breech and the other in head presentation is by no means unusual. In 51 such cases of simultaneous engagement, there were 12 where both heads entered the pelvis at practically the same time.

GYNECOLOGY

UNDER THE CHARGE OF

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Vulvovaginitis.—Vulvovaginitis has been termed a free lance disease by STEIN (*Surg., Gynec. and Obst.*, 1923, **36**, 43), who points out that

although the physicians in diverse specialties accept the condition for treatment, there is no uniformity in diagnostic procedure or mode of therapy, nor is there any accepted plan of procedure endorsed by a single specialty. The treatment of the condition in the hands of various specialists varies from simple hygienic measures to the most painstaking local applications, but is for the most part empirical and frequently irrational. About a year ago, a joint meeting was called of the gynecological and genito-urinary departments of the Michael Reese Hospital Dispensary to discuss the problem of the disposition of the vulvovaginitis patients. No agreement could be reached. One physician claimed that all the cases were gonorrheal, another said that they were never gonorrheal, one held that they always arose from contact, and another believed that filth was the sole cause. With such diversity of beliefs as to etiological factors, naturally no plan of procedure could be outlined, and it was decided to investigate the cause of vulvovaginitis, clinically and bacteriologically. The conclusions which the author has reached as a result of his investigation are that vulvovaginitis is an infection which is frequently gonorrheal in origin, but may even in purulent varieties be non-specific. Filth unquestionably plays a part in predisposing to the infection and may be the chief cause in the milder types. Diagnosis rests upon clinical evidence of the disease and smear examinations made by an expert. Cultures prove positive in about 50 per cent of gonorrheal cases and are therefore not requisite for diagnosis. Purulent vulvovaginitis should be vigorously treated by an approved method and a daily tub bath is an aid to local treatment, and in mild non-gonorrheal cases is all that is required for cure. Determination of cure rests upon the disappearance of clinical evidence of the infection, three negative smears at intervals of one week after suspending treatment and a period of observation equal in time to the duration of the treatment. Summarizing his results of treatment, the author states that gonorrheal vulvovaginitis can be cured by daily injections of 1 per cent mercurochrome ointment into the vagina in an average of 9.7 weeks. Suspicious cases can be cured in 6.5 weeks, and non-gonorrheal cases in 5 weeks. In 2 gonorrheal cases recurrence occurred after contagious disease (chicken pox, measles). In 1 non-gonorrheal case, recurrence occurred from no apparent cause three months after treatment was suspended. It is of interest to note that in six instances sisters were affected at the same time, and in each instance a remarkable similarity in clinical course, bacteriological findings and response to therapy was noted.

Technic of Vaginal Drainage.—In discussing the technic of vaginal drainage of pelvic infections, GIRARD (*California State Jour. Med.*, 1923, **21**, 9) states that in order to make the opening in the posterior fornix a most simple procedure and "fool proof" he has devised a clamp approximately 25 cm. long with a double curve and when closed the end forms an oval ball 3.5 cm. wide and 2.5 cm. high. The anterior surface of the ball is grooved transversely, and this groove the operator feels through the stretched tissues of the posterior fornix, and makes his incision directly down on the ball of the instrument, thus avoiding any possibility of injury to the rectum, which is held posteriorly by the lower half of the ball while the back of the cervix is pushed forward

by the upper half. If a large opening is desired, a crucial incision can be made at will, using the ball as a guide. After the incision is made, the clamp is opened by the assistant and the drainage material is placed between the jaws of the guide and withdrawn into the vagina. Gauze drains will cause more outpouring of lymph than rubber tubing or cigarette drains, which is to be desired, but they have the disadvantage of becoming entangled in the tissues when the lymph coagulates and causing injury to the granulations when the guaze is removed. In order to overcome this objectionable feature of gauze, Girard uses paraffine gauze, which can be laid in strips between the plain gauze and the wound or can be used in the form of a casing for a cigarette drain which he has devised, the ends of the paraffine casing being made fan shape so as to cover any large denuded area which cannot be covered by peritoneum and thus protect the denuded area from becoming adherent to omentum, intestines or adjacent organs and which, when removed five or six days later, will not adhere to the protected area which by that time has become well endothelialized.

Cystoscopy in Urinary Tuberculosis.—In commenting upon the value of cystoscopy in the diagnosis of urinary tuberculosis, BALL (*Brit. Jour. Surg.*, 1923, **10**, 326) reminds us that renal tuberculosis is a slowly progressive disease which unfortunately may not give rise to symptoms of a sufficiently definite character to cause the affected person to seek advice until, it may be, considerable destruction of the affected organ has taken place; in fact, the involvement of the bladder, with coincident symptoms, may be the first indication of this serious malady. Symptoms indicating involvement of the kidney are of slow development and may be absent altogether, even when that organ has been completely destroyed, dysuria associated with frequent micturition at night as well as by day being commonly the first evidence of disease. Ability to recognize the appearances seen in the bladder by cystoscopic examination is therefore of great importance in the diagnosis of renal tuberculosis, more especially in demonstrating which kidney is at fault, as in 80 to 90 per cent of cases, so it is stated, one kidney only is affected in the early stages. It is frequently, from the technical point of view, a difficult matter to carry out a satisfactory cystoscopical examination in this condition. Prior to the appearance of tuberculous lesions in the bladder mucosa little difficulty presents itself, but when the latter exist, then, owing either to a spasm in the early stages or to infiltration of the muscle of the bladder wall in the later stages, it is often impossible to make a thorough investigation unless the patient is under a general anesthetic, the distention of the bladder with fluid in sufficient amount causing severe pain. It is the author's practice, whenever a tuberculous infection is suspected, to adopt this procedure; even then, extreme care must be taken to avoid over-distention of the bladder, otherwise hemorrhage may be caused and irreparable damage supervene, such as the lighting up of a latent lesion or the introduction of a secondary infection, results easily induced by even a slight trauma. There is, moreover, a further difficulty in diagnosis from the pathological aspect, namely, that lesions may have assumed such characters, especially in the presence of secondary infection with other bacteria, as to render them indistinguishable

from those associated with other forms of cystitis; even in the absence of the latter, the bladder may have become so extensively involved in the tuberculous process as to make it impossible to identify the original site of the bladder lesion, which may be the only clue indicating its possible origin from the kidney. For this reason it is an extremely important matter that an early investigation of the bladder should be carried out in all suspected cases of infection: (1) In order to define the existence of any abnormality in the effluxes from the ureteric orifices or in the bladder mucosa; and (2) to recognize the position of such changes in order to obtain an indication of the site of the primary lesion. The latter point requires emphasizing, for the finding of tubercle bacilli in urine containing blood or pus, with symptoms of cystitis, only indicates the presence of urinary tuberculosis; it offers no suggestion as to the requisite treatment. This the cystoscope alone can give in the absence of localizing symptoms, which may be completely absent, but even if present, confirmation is always necessary. Some authors state that it is unwise to carry out cystoscopical examinations in cases of tuberculous cystitis owing to the liability of causing further damage. It is agreed that it is unwise to employ this method of investigation during the acute symptoms of bladder infection, or more often than is necessary in the chronic stage; but it is obviously important that an exact location of the bladder lesions should be made as soon as possible, in order that the correct treatment may be determined. This information cannot be obtained without a cystoscopical examination, which should therefore be insisted upon. This advice of the author is quoted with the hearty endorsement of the editor in the hope that the forceful dissemination of such knowledge may be the means of saving many lives by bringing to early operation the early cases of renal tuberculosis, which can only be done by the careful investigation of all pyurias and dysurias of more than brief duration.

End-results of Interposition Operation.—Many operations are fascinating to watch or perform, but in the field of gynecology it is doubtful whether any other operation interests the student or the novice more than the interposition operation for prolapse. Whether you would give the credit for the invention of this procedure to Wertheim, Schauta or to our own Watkins (where it properly belongs), the fact remains that it is an ingenious operation *per se*. However, the thinking, conservative surgeon looks at an operation from another angle, namely the end-results. What are the end-results after this operation? SHAW (*Surg., Gynec. and Obst.*, 1922, **34**, 394))has investigated this subject in 118 cases operated upon since 1900 in the gynecological department of the Johns Hopkins Hospital. Of this number he was able to trace 58 patients, 40 of whom were completely relieved of their symptoms, 13 were not improved, 3 had died after leaving the hospital and 2 died in the hospital, 1 from pulmonary embolism on the twelfth day and the other from a hemorrhage of the uterine artery on the tenth day. These results, 13 failures out of 53 cases, the author admits are not brilliant, although he thinks they might be partly due to the fact that most of the patients were of the dispensary type, from whom failures are heard of more readily than successes. With increased

experience in selection of cases in which the operation is suitable and with suitable modifications of the technic in the individual case, much better results have been obtained, as there has only been one failure since 1915 in 40 operations, 21 of whom have been followed. The author concludes that the operation is limited to a small group of cases, near or subsequent to the menopause, where an abdominal suspension, combined with a thorough repair of the perineal floor is contraindicated.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Studies on the Pneumococcus. Acid Death Point of the Pneumococcus.—By seeding 5 cc of an isotonic broth, whose hydrogen-ion concentration ranged in eight steps from pH 4.47 to 7.8, with two drops of a saline suspension of washed living pneumococcus, and by transplanting on blood serum after varying intervals of inoculation, LORD and NYE (*Jour. Exper. Med.*, 1922, **35**, 685) found that at a pH of 4.47 no living bacteria were obtained after an interval of one hour, and at a pH of 5.15 living organisms were obtained after one hour but not after two, while at pH 5.78, they were living after two hours but not after three, whereas at pH 6.33 living pneumococci were encountered after six hours, At a pH of 6.63 to 7.80, the transplants were positive from eight to ten days, indicating that the greater the acidity, the more rapid the death.

In a second communication (*Jour. Exp. Med.*, 1922, **35**, 689) it was learned, from the results of a series of titrations, that suspensions of living pneumococci (Type I, II and III) in approximately isotonic standard solutions and bouillon with pH varying from 4 to 8 after incubation show dissolution of bacteria in those solutions having a pH higher than about 5, the dissolution being most marked at a critical range of about 5 to 7. While some dissolution was encountered toward the more alkaline end, no dissolution occurred at the most acid end of the scale. Although dissolution took place at incubation, room and ice-box temperature, it was less marked at the latter. Dissolution also occurred in standard pH solutions with pneumococci allowed to grow and die out in glucose bouillon, but, unlike living organisms, the dissolution was progressive from the acid toward the alkaline end of the scale. Pneumococci killed by heat for one hour underwent less dissolution than living organisms, while those killed by heat at 100° C. for five minutes did not undergo dissolution, and the addition of fresh human

serum to the pneumococcal suspensions at varying pH prevented dissolution. Dissolution occurred more rapidly at pH 6.1 in standard solutions in which large numbers of pneumococci had been previously dissolved than in fresh standard solutions at the same pH. The authors believe that this dissolution can be ascribed to an enzyme derived from the bacteria themselves, calling attention to the fact that under similar conditions S. viridans and hemolyticus and S. aureus did not dissolve.

In a third study (*Jour. Exp. Med.*, 1922, **35**, 699) suspensions of Type I, II and III pneumococci were added to the cellular material from a pneumonic lung due to Type I pneumococcus at varying hydrogen-ion concentrations. All types of pneumococci were found to undergo dissolution at a pH of 6.95 and 5.5, but not at a pH of 4.5, whereas S. hemolyticus and viridans do not dissolve. The authors believe that an enzyme derived from the bacteria themselves or from the cellular material may be the cause of the dissolution.

Finally (*Jour. Exp. Med.*, 1922, **35**, 703), the effect of bile at varying hydrogen-ion concentration on the dissolution of Type I, II and III pneumococci was determined by adding pnemococcal suspensions to fresh beef bile. After incubation it was found that the dissolution of the pneumococci occurred most rapidly in the bile at a slight alkaline reaction (pH 6.1). The authors believe "this is probably due to death of the organisms and activation of the endocellular enzymes at the optimum hydrogen-ion concentration."

Melanoblastoma of the Nail-bed (Melanotic Whitlow).—HERTZLER (*Arch. Dermat. and Syph.*, 1922, **6**, 701) reports 2 cases of melanoblastoma of the left thumb nail-beds in women, aged sixty-four and fifty-four years respectively. In 1 case there was a history of slight injury a year and a half previously, while in the other no record of trauma could be elicited, the condition beginning as a black spot under the nail four years previously. In both, too, the nail was absent, having been supplanted by a blue-black ulcerating tumor, which had eventually become painful and sensitive. The border of the tumors was deeply pigmented. No lymphatic involvement was found in either case. Amputation was instituted in each instance, and at the end of two years in the first case and two months in the second, no evidence of recurrence could be demonstrated. The author was able to collect 17 additional similar cases from the literature. He thinks that the term "melanoblastoma of the nail-bed" is more accurate than "melanotic whitlow" and should supplant it.

Experimental Rickets in Rats. IV. The Effect of Varying the Inorganic Constituents of a Rickets-producing Diet.—Having previously shown that rickets could be produced in rats by a diet composed of patent flour, calcium lactate, sodium chloride, and ferric citrate, and that it could be prevented by the substitution of 0.4 per cent basic potassium phosphate for an equal percentage of calcium lactate, PAPPENHEIMER, MCCANN and ZUCKER (*Jour. Exper. Med.*, 1922, **35**, 421) report the above changes which were produced in additional rats by varying the inorganic constituents of the diet. It was found that rachitic bone lesions occurred in rats who had received a diet containing an excess of calcium but deficient in phosphates, while similar lesions

followed a diet deficient in calcium but containing an excess of phosphates and that atypical rickets was produced by a diet deficient in both calcium and phosphates, whereas inorganic salts other than calcium or phosphate seemed to be without influence upon the development or prevention of rachitic lesions. The minimal amount of phosphates required for calcification of young growing rats under the conditions of these experiments was about 160 mgm. per 100 gm. of diet. An excess of calcium was not necessary to the production of the rachitic lesions and a reduction of the calcium lactate in a given diet to 0.6 per cent (111 mg. of Ca per 100 gm. of diet) resulted in the development of typical rickets. Adult rats reacted to a deficiency of phosphate in the diet by the production of calcium-free osteoid in abnormal amount about the spongiosa and cortex and there was not produced any alteration of the epiphysial cartilage, as in growing animals.

Experimental Rickets in Rats. V. The Effect of Varying the Organic Constituents of a Rickets-producing Diet.—Under conditions of experimentation similar to those previously employed, PAPPENHEIMER, MCCANN and ZUCKER (*Jour. Exper. Med.*, 1922, **35**, 447) continued their investigation of the prevention and production of rachitic bone lesions in rats receiving a diet in which the organic constituents were modified. It was learned that casein phosphorus did not prevent completely the development of rickets when substituted in a given diet in amount equivalent to a protective dose of basic potassium phosphate; that the protection given by lecithin or yeast was proportional to the phosphorus content, and that vitamin A, in the form of butter or butter fat, to the amount of 10 per cent of the diet, neither prevents or cures rickets; that the substitution of 10 per cent of egg albumen in the given diet improved the nutrition but did not prevent rickets, whereas the addition of meat promoted normal growth and bone formation, although a diet of only meat and flour was inadequate for proper growth, leading to bone changes comparable to those observed on a diet low in calcium, but not in phosphorus. The authors state that "a diet has been found which contains the necessary food elements for approximately normal growth and in which the only known deficiency is phosphorus. This leads regularly to the production of rickets."

Do Species Lacking a Gall-bladder Possess its Functional Equivalent?—Some closely related species of animals have a gall-bladder while others do not. It is present in the cow, sheep, goat, hog and wild boar, and absent in the horse, deer and peccary. The hawk and owl possess it, while the dove does not, and among rodents, the mouse is found with the organ, the rat without it. Furthermore, the gall-bladder is not found in the pocket gopher, whereas it occurs in the striped gopher. Again it can be present or wanting in the giraffe. Having previously shown that the gall-bladder concentrates bile greatly and the ducts dilute it slightly, MCMASTER (*Jour. Exp. Med.*, 1922, **35**, 127) conducted a series of experiments on rats (animals devoid of gall-bladder) and mice which possess the organ, by determining the amount of pigment normally in the species and after ligating the bile ducts. Both the rat and the mouse were found to secrete larger quantities of bile than the dogs and cats, but less than guinea-pigs and rabbits. Bladder bile of the mouse was found more concentrated than common duct bile

and stasis bile showed a great increase in pigment content, whereas in the rat, stasis bile never became more concentrated than normal, indicating that the gall-bladder is absent from the rat not only in form, but in at least one of its important functions, that of a reservoir. On the other hand, although rat bile did not undergo condensation of bulk after leaving the liver, it contained about eight times as much pigment as did liver bile in the mouse, which becomes concentrated in the gall-bladder, so that, in either animal the bile as it reaches the intestine, may not be dissimilar, certainly in pigment, and perhaps in substances useful for digestion, although the author states that little can be said concerning the latter at present.

A Three Months Old Strain of Epithelium.—Although the cultivation of epithelium appeared to be more difficult than that of connective tissue, it seemed probable to FISHER (*Jour. Exper. Med.*, 1922, **35**, 367) that if epithelial tissue could be obtained free from connective tissue cells they could be kept in pure culture indefinitely, Accordingly it has been possible to cultivate, *in vitro*, a strain of pure epithelial cells from that portion of the iris of a chick embryo which adheres to the extirpated lens on the free surface of plasma clot under a film of embryonic tissue juice. The strain is now three months' old and the epithelial cells have not differentiated, growing as a pavement membrane and have retained their epithelial characteristics. The rate of proliferation is increasing, every culture doubling in size after three or four days. Several plates are presented to show numerous mitoses and different stages of amitotic cell division.

Significance of the Hemosiderosis of Pernicious Anemia.—Many believe that pernicious anemia is due to an injurious agent derived from the gastro-intestinal tract, citing the marked siderosis of the liver parenchyma occurring during pernicious anemia as evidence to indicate that pathological blood destruction is localized within the portal tributaries. After experimentation on young rabbits, MCMASTER, ROUS and LARIMORE (*Jour. Exper. Med.*, 1922, **35**, 521) have shown that a similar siderosis can be produced by varying the amount of pigment set free in the general circulation. As a result of these findings, the authors believe that the selective deposition of the hemosiderin in the hepatic parenchyma during pernicious anemia does not constitute evidence that there is a hemolytic cause for the disease located in the portal region. The hemoglobin was prepared from the rabbit corpuscles and was injected six days out of seven in concentrated watery solution, subcutaneously, into the flanks and the abdomen, in doses ranging from $\frac{1}{4}$ to $\frac{1}{150}$ of that normally possessed by the animal over a period from thirteen to one hundred and two days. Blocks from the liver, kidney, spleen and red bone marrow were fixed in alcohol and stained with ammonium sulphide and in duplicate by the combined ammonium sulphide-potassium ferrocyanide method of Nishimura. The criterion employed to gauge the degree of siderosis was the appearance of the tissue under the microscope. When a daily dose less than $\frac{1}{90}$ of the approximate quantity of pigment in circulation was given, even for many weeks, practically no siderosis was found. With slightly larger; long-continued injections, there was a stippling with hemosiderin of the hepatic parenchyma. As in pernicious anemia this stippling was

most pronounced near the periphery of the lobule. With still larger inoculations, both the liver and tubular epithelium of the kidneys became equally siderosed, and when the hemoglobin doses were massive the liver was negligibly pigmented in contrast to the heavy deposits in the kidneys, at which times amorphous material giving the iron reaction was seen lying free in the glomerular capsule and in the lumina of the upper tubules. No consequential siderosis was encountered in the spleen or in the bone marrow. Attempts to repeat the work with dogs were not as satisfactory. However, in both dogs and rabbits the renal siderosis affected especially the cells of the proximal convoluted tubules and of the ascending limb of Henle's loop, as seen in pernicious anemia but not in hemochromatosis. The authors point out that many types of blood destruction which are systemic in origin, become portal in completion, a circumstance which may well take place in pernicious anemia, and that no matter how suggestive various factors encountered in this disease may seem, it is "a good policy to box the compass of possibilities in the consideration of so obscure a disease as pernicious anemia, rather than look for enlightenment in a fixed direction."

A Simple Quantitative Precipitation Reaction for Syphilis.—KAHN (*Arch. Dermat. and Syph.*, 1922, **5**, 570) describes a precipitation method based on the employment of syphilitic serum with alcoholic extract antigens of heart muscle. The author has found the test very simple and delicate, having the added attraction that the diluted antigens are quite stable, that the strongly positive serums usually show spontaneous precipitation, the test being complete after three hours in the water-bath and that the end results can be read with relative ease. The antigen consisted of an alcoholic extract of dried pig or beef heart free from ether extractives and cholesterinized by adding 400 mg. of cholesterin to 100 cc of alcoholic antigen. The proper dilution of the antigen was ascertained by adding, rapidly, various amounts of salt solution, that diluted antigen which was milky but opalescent and free from precipitate being the desired one. The serums were inactivated by heating at 56° C. for thirty minutes. To perform the test, 0.3 cc inactivated serum were mixed with 0.1 cc of the diluted antigen in a small tube, gently shaken and incubated at 37.5° C. The results were read after one and three hours incubation, the presence or absence of precipitation determining the positivity or negativity of the reaction. Of 1119 serums examined by the precipitation and Wassermann methods, 213 were positive, 20 were doubtful, and 767 were negative by both methods, giving a total of 1000 specimens or 89.36 per cent showing agreement. 7 positive reactions were doubtful in the precipitation test; 40 doubtful Wassermann reactions were positive; 30 doubtful Wassermanns reactions were negative; 21 negative Wassermann reactions were doubtful; the total 98 specimens (8.75 per cent) showing relative agreement. 14 negative Wassermann reactions gave weakly positive precipitation reactions; 7 weakly positive Wassermann reactions gave negative precipitation reactions, giving a total of 21 (1.87 per cent) specimens which did not check. In not a single instance did a four plus or a three plus Wassermann reaction show a negative precipitation, or a positive precipitation show a negative Wassermann. The author hopes that the simplicity and ease with which the test can be performed will attract others to investigate it in conjunction with clinical studies.

HYGIENE AND PUBLIC HEALTH

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Pellagra.—Amino-acid Deficiency Probably the Primary Etiological Factor.—GOLDBERGER and TANNER (*United States Public Health Reports*, 1922, **37**, 462) briefly summarize the more important part of the evidence proving diet to be the primary controlling factor in the prevention and causation of pellagra. Cases of pellagra are reported that were observed to occur in individuals who were known to have consumed daily, during a period of not less than two and one-half months immediately before the onset of the distinctive eruption, what is judged to have been a liberal supply of mineral elements and the known vitamines, which would indicate that a deficiency of these dietary factors is not essential in the causation of the disease. These factors having been thus excluded, the dominating role of diet in the prevention and causation of pellagra must be referred primarily to the character of the protein (amino-acid) supply; this being the only other dietary factor at present known to be necessary to physiological well-being. On the assumption that all the dietary factors essential in human nutrition are known, it may be concluded that the essential etiological dietary factor is a specific defect in the amino-acid supply, probably in the nature of a deficiency of some special combination or combinations of amino-acids. There is reason to believe that besides the specific amino-acid defect, pellagra-producing diets may, and probably frequently have other more or less serious faults, including non-specific amino-acid deficiencies, which may operate as accessory etiological factors. In some preliminary therapeutic trials with amino-acids the dermal lesions in each of 2 cases seemed to show a markedly favorable reaction to cystin; and in a third case a steady gain in weight, with some improvement in diarrhea, accompanied the administration of both cystin and tryptophane.

Direct Injection of B. Typhosus into the Gall-bladder.—BECKWITH (*Jour. Infect. Dis.*, 1922, **31**, 468) states that the older idea that presence of B. typhosus within the gall-bladder in a typhoid carrier is due to direct invasion of the bacilli by way of the common and cystic ducts from the duodenum no longer seems tenable. However, there is still strong reason to believe that this may be the path of invasion for Entameba dysenteriæ and for certain parasites. One may conceive that a foreign toxin-producing body within the bile may be able to produce a generalized condition in the body, as the wall of

the gall-bladder has been demonstrated to comprise an active permeable and concentrating mechanism. With this possibility in mind it was attempted to learn whether the introduction of B. typhosus within the gall-bladder directly is followed by the appearance of bacilli and of agglutinins in the circulation. The author found that injection of B. typhosus directly into the gall-bladder of the rabbit is followed by prompt appearance of agglutinins within the circulation. This response is stimulated by dead as well as by living organisms. Typhoid bacilli implanted within the gall-bladder pass through the lining epithelium and appear shortly in other organs, such as the spleen, liver, lung and kidney, but they are not isolated from the peripheral circulation. It seems likely that lymph is at least partially responsible for this distribution. Migration of B. typhosus through the epithelium into the tunica is attended after appropriate lapse of time by the formation of lesions which are characteristic of those found in the typhoid carrier.

Experimental Botulism in Dogs.—GRAHAM and ERIKSEN (*Jour. Infect. Dis.*, 1922, **31**, 402) found that unfiltered type A toxin of Clostridium botulinum proved fatal to dogs in doses of 0.1 cc or more administered subcutaneously. Type A spores, detoxicated by washing and heating, produced no noticeable effects when injected subcutaneously into dogs. Feeding relatively large amounts of unfiltered type A toxin (100 cc) produced illness and death in dogs only when food had been previously withheld for forty-eight hours. The effects of other forms of artificially induced fatigue were not determined. The symptoms of type A intoxication included loss of appetite, muscular weakness, languor, prostration, salivation, congestion of the mucous membranes of the mouth, and respiratory disturbances. Type A antitoxin apparently protected dogs against lethal amounts of toxin. Unfiltered type B toxin of Clostridium botulinum administered intravenously and subcutaneously in liberal amounts failed to induce manifest symptoms. The internal organ and muscle tissues of horses and pigs which had died of type A botulism were consumed by dogs without ill effects. Dogs appear to be satisfactory animals for differentiating A and B toxins of Clostridium botulinum following subcutaneous injection.

Isolation of Anthrax Bacillus from a Shaving Mug.—VINCENT (*Jour. Infect. Dis.*, 1922, **31**, 499) reports a case of anthrax of the neck, and concludes from the results of examination of a shaving mug that it is evident that the shaving brush in all probability harbored anthrax bacilli, and that the spores or bacilli adhered to the mug after the removal of the brush, showing again the great resistance of this organism.

Interepidemic Influenza.—JORDAN (*Am. Jour. Hygiene*, 1922, **2**, 325) calls attention to the conspicuous place occupied by influenza among the reported causes of death between the epidemics of 1890 and 1918, and brings forward a number of interesting facts. The lack of uniformity in the clinical picture of influenza makes the comparison of the symptoms of epidemic and interepidemic cases of doubtful value,

and the term has undoubtedly been used very loosely. Before 1890 the designation influenza was rare in health reports of American cities, but in that pandemic year it became conspicuous and has remained more or less in evidence since that time. In certain localities there is indicated a tendency to report as influenza deaths that in other localities would be reported as pneumonia or bronchitis. There is no doubt about the comparability of the pandemics of 1890 and 1918. Whether the so-called influenza of interepidemic years is the same disease with these great epidemics is an important question, and until the causal agent or its effects can be recognized a considerable measure of uncertainty will probably continue to exist. But certain kinds of indirect evidence may be interpreted to indicate that the so-called influenza of interepidemic years is at least in part different from the influenza of the great epidemics of 1890 and 1918: (1) In the epidemic of 1918 the greatest mortality was at the ages twenty-five to thirty-five. During the years 1900–1917 less than 10 per cent of the deaths were in this age period, more than 50 per cent being in persons over sixty. (2) In the 1918 epidemic there was a relatively increased mortality in the white race as compared with the negro, in contrast to the higher mortality among negroes in the preëpidemic period. (3) The mortality was higher in white males than in white females, as contrasted with the higher mortality among females in preëpidemic years. (4) There was a relatively increased mortality in colored males during this time as compared with colored females. During 1918 the increase in reported deaths from influenza was accompanied by an increase in deaths from pneumonia, as might be anticipated. In the preëpidemic years (1900–1917) there were notable divergences in the two rates. Too much weight should not be attached to this lack of correspondence between pneumonia and influenza in interepidemic years, since the pneumonia death rate is affected by a number of inconstant factors. The author concludes: Evidently many deaths reported as influenza in interepidemic years are not due to the same microbic causes as those occurring in epidemic years. Is this true of all? May there still be a residue of cases and deaths from true influenza which keeps a thread of continuity between the great outbreaks? The question probably cannot be answered until the causal agent is identified. Meanwhile localized outbreaks and even individual cases of mild respiratory disease should be given searching study.

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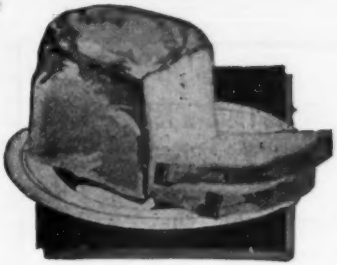

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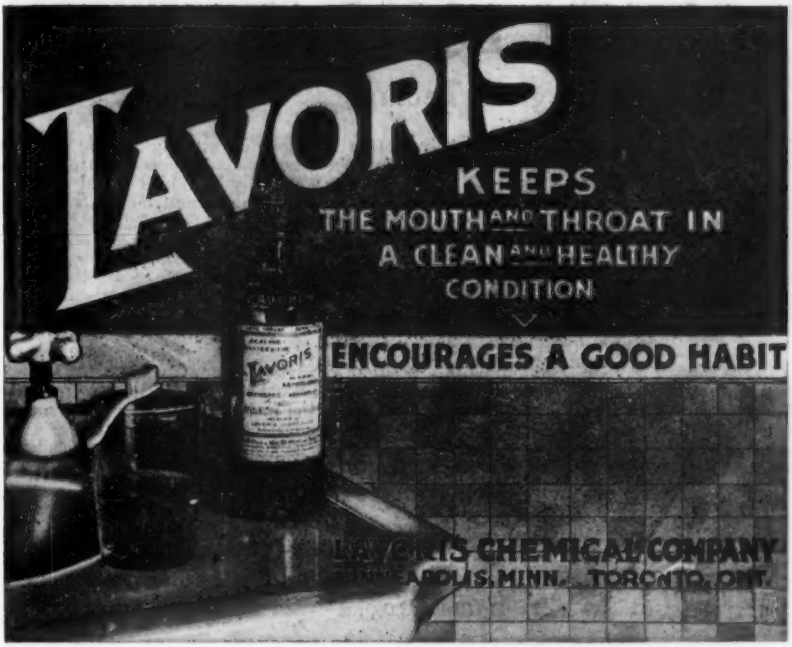

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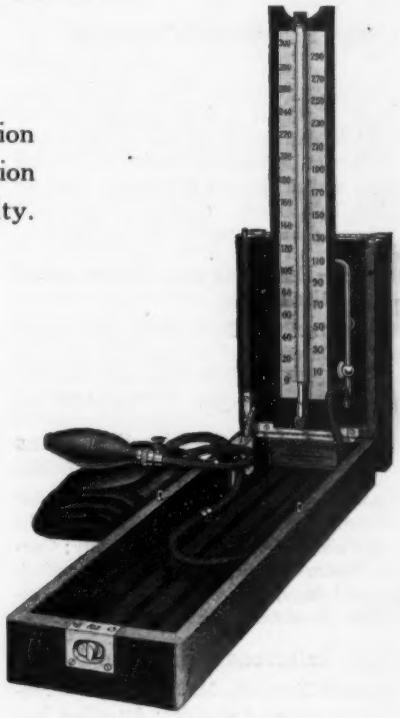

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